The Impact of Retail Sector Delivery of Artemether-Lumefantrine on Effective Malaria Treatment of Children Under Five in Kenya

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The Impact of Retail Sector Delivery of Artemether-Lumefantrine on Effective Malaria Treatment of Children under five in Kenya

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A thesis submitted to the Open University, Mathematics and Statistics Discipline in partial fulfilment of the degree of Doctor of Philosophy

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ABSTRACT

Background: With a low proportion of children receiving the first line treatment for suspected malaria, it has been proposed that artemisinin based combination therapy be subsidised in the private sector in order to improve affordability and access. This thesis presents an evaluation of a pilot subsidy mechanism in Western Kenya.

Methods: The primary objective was to evaluate the impact of providing subsidized artemether-lumefantrine (AL) through trained retailers, on the coverage of prompt effective anti-malarial treatment for febrile children aged three to 59 months. I used a cluster-randomised, controlled design with nine control and nine intervention sublocations, equally distributed across three districts. Provider, mystery shopper and household cross-sectional surveys were conducted at baseline and one year later. Data were analysed based on cluster-level summaries, comparing control and intervention arms, while adjusting for covariates. On average details of 2,706 children and 564 retail outlets were captured per year.

Results: Provider survey and mystery shopper data showed that at follow-up a significantly greater percentage of retailers stocked and dispensed AL, and knew that AL was the first line treatment for uncomplicated malaria in the intervention arm compared to the control. Significantly fewer retailers stocked antimalarial monotherapies. Household survey data showed that an average of 29% of children had experienced fever within the previous two weeks. Within this sample, the percentage receiving AL on the same day or following day of fever developing at follow-up was 25.0% points higher in the intervention arm than in the control arm, a statistically significant difference. However, adherence to dosing for AL purchased in the retail sector and advice given to caretakers by retailers remained unchanged post-intervention.

Conclusion: Overall, subsidizing ACTs in the retail sector can significantly increase ACT coverage in rural areas. Further research is needed on ways to improve counselling and adherence as well as on the impact and cost-effectiveness of such an intervention at a national scale.

ABBREVIATIONS AND ACRONYMS

ACT	Artemisinin Combination Therapy
ADR	Adverse Drug Reactions
AL	Artemether-Lumefantrine
AMF-m	Affordable Medicines Facility- malaria
CFW	Child and Family Wellness Clinics
CHW	Community Health Worker
CI	Confidence Interval
CORPs	Community Owned Resource Persons
CQ	Chloroquine
DHMT	District Health Management Team
DHS	Demographic and Health Survey
DO	District Officer
DOMC	Division of Malaria Control
EA	Enumeration Area
FGD	Focus Group Discussions
GF	Global Fund
GIS	Geographical Information System
GPS	Global Positioning System
HMM	Home Management of Malaria
iCCM	Integrated Community Case Management
IEC	Information, Education and Communication
IMCI	Integrated Management of Childhood Illnesses
ITN	Insecticide Treated Net
IV	Instrumental Variable
KSH	Kenya Shillings
KWTRP	KEMRI Wellcome Trust Research Programme
MOH	Ministry of Health
NGO	Non-Governmental Organisation
NO/ N/ n	Number
OTC	Over the Counter
PCA	Principal Components Analysis
POM	Prescription Only Medicine
PPB	Pharmacy and Poisons Board
PSI	Population Services International
RBM	Roll Back Malaria
SES	Socio-economic status
SD	Standard Deviation
SFH	Society for Family Health
SHEF	Sustainable Healthcare Enterprising Foundation
SP	Sulphadoxine-pyrimathamine
SRP	Suggested retail price
USD	United States Dollars
WHO	World Health Organisation

ROLES

The author participated in the conceptualisation and outline of the study design. The author was responsible for the design of the data collection tools, implementation of data collection activities, design of the analysis plan and the analysis carried out in Chapters 5 (the Provider Survey) and 7 (the Household Survey). Chapter 6 (the Mystery Shopper Survey) was analysed and written up by the author's assistant (Sarah Kedenge) under the author's supervision. The Geographical Information Systems (GIS) analysis described in Chapter 4 (Study Site and Methodology Overview) was carried out by a member of the KEMRI Wellcome Trust GIS team (Victor Alegana). Chapter 7 was published in the PLoS Medicine Journal:

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CHAPTER 1

INTRODUCTION

Artemisinin-based combination therapies (ACT) are generally accepted as the best treatment for uncomplicated malaria and have been widely adopted as national policy throughout Africa. However, usage of ACTs remains very low, leading to calls for radical solutions to improve access to effective malaria treatment, including expansion of home management of malaria (HMM). Prominent among these strategies is a proposal to subsidize ACTs in the private sector, proposed by the Institute of Medicine (IOM) committee in their report "Saving Lives, Buying Time" in 2004 (Arrow *et al.,* 2004). This has led to numerous discussions at the international level on whether and how this should be implemented in practice. Limited experience to date indicates that ACT subsidies can lead to increased ACT uptake and decreased use of inappropriate monotherapies, but many important questions remain unanswered. This thesis aims to address these information gaps by presenting the results of a cluster randomised controlled trial evaluating the impact of a package including ACT subsidies, retailer training and community awareness on ACT coverage, price and adherence in a high malaria transmission area of Western Kenya. This introductory chapter presents the background to and rationale for the research, the objectives, and outlines the organisation of the thesis. Chapter 2 reviews the evidence on the effectiveness of HMM and chapter 3 explores different evaluation methods involved in assessing public health interventions.

1.1: RATIONALE

1.1.1: Malaria Background

Malaria remains an important health problem with an estimated 2.37 billion individuals living at risk of transmission of *Plasmodium falciparum*, the most virulent of the malaria causing plasmodium species (Guerra *et al.,* 2008). It has been estimated that in 2007 there were between 349 to 552 million clinical cases of *P.falciparum* malaria (Hay *et al.,* 2010). *P. falciparum* contributes to 90% of the malaria burden in Africa, and 1 million childhood deaths per year are a direct consequence of the parasitic infection (Snow *et al.,* 2005; Snow *et al.,* 1999).

The creation of the Roll Back Malaria (RBM) global partnership in 1998 brought international hope after a long period where malaria control strategies had received a relatively low priority on the global stage. The RBM created a mandate to increase international awareness of malaria and to rally support in the control of the disease (RBM, 2005). It aims to do this by working closely with countries affected by the disease, supplementing and strengthening health services therefore, increasing access to prevention and treatment measures (Malaria Consortium, 2002). One of its core targets was that '80% of those suffering from malaria should receive appropriate treatment within 24 hours' (World Health Report, 2008). Reaching this target is still a great challenge for Africa, partly because of the development of drug resistance of the malaria parasite to first line therapies, such as sulphadoxine-pyrimathamine (SP) and amodiaquine (Nchinda, 1998). By contrast, artemisinin derivatives are currently considered very effective in the treatment of P. *falciparum* malaria, the most virulent of the malaria plasmodium species. It is thought that the rate of development of resistance to artemisinin derivatives will be much slower than that for other antimalarial monotherapies because of their short half-life, and their use in combination with other treatments (de Vries & Dien 1996; White *et al.,* 1999). When used in combination with other effective anti-malarial monotherapies, ACTs have been shown to be well tolerated, to lower transmission rates within communities by reducing gametocyte loads, and have demonstrated cure rates of over 90% (IASG, 2004). The migration of countries from less effective antimalarial monotherapies such as chloroquine (CQ) and SP to ACTs was not straight forward, and this transitional delay is thought to have contributed to tens of thousands of childhood deaths per year (Attaran *et al.,* 2004). Although evidence was available to show the therapeutic advantage of ACTs over failing monotherapies, there was resistance from the Global Fund (GF) who were not keen on funding country policies that were based on ACTs since these were shown to be ten times more expensive than monotherapies (Attaran *et al.,* 2004). This was compounded by a lack of direction on international malaria treatment guidelines by the WHO (Attaran *et al.,* 2004) and poor country sensitivity data on suggested alternative first line treatments (Amin *et al.,* 2007).

Since the creation of the RBM global partnership, significant strides have been achieved in controlling malaria. There has been a large increase in funding to support malaria control initiatives. By the end of 2009, the GF had approved \$5·3 billion for 191 malaria grants in 82 countries. Such funding has contributed to a 17% rise in the use of ITNs in just five years and widespread use of ACTs, with every malaria-endemic country adopting it as a first-line treatment (Noor *et al.,* 2009; Snow & Marsh, 2010). ACTs are now generally accepted as the best treatment for uncomplicated *P. falciparum* malaria (WHO, 2006). However, usage remains very low, with only 16% of febrile children under the age of 5 years receiving ACTs in 2008 (World Malaria Report, 2009).

A correlation has also been observed between increase funding and a significant decrease in the incidence of severe malaria, such as in the coast of Kenya where severe malaria cases dropped by over 90% in just five years (Okiro *et al.,* 2009; Omera *et al.,* 2008). These observations can be partly attributed to the enhanced control and prevention activities, however it is thought that more complex factors are responsible (Snow & Marsh, 2010). Substantial gains have been made in reducing the burden of malaria across parts of Africa, however gaps still remain. Although malaria has been observed to be decreasing in certain regions, this is not the case across the continent where some areas have either shown no change or even an increase in the number of cases or the percentage of population at risk (Snow & Marsh, 2010; Okiro *et al.,* 2009). More funding is required to expand effective control initiatives to reach the recommended target expenditure of \$4.46

per person living in Africa per year, estimated to be needed to achieve full effective coverage of efficacious intervention strategies (Teklehaimanot *et al.,* 2007).

1.1.2: The Kenyan Health Care System

Kenya's health care system can be described as pluralistic, where healthcare facilities are owned and funded by a wide variety of institutions such as the government, private commercial and not-for-profit institutions (Table 1.1). The government funds and is in direct control of all public sector health care which consists of government health care facilities and community owned resource persons (CORPs) or community health workers (CHWs). In 1997, it was estimated that the public sector operated around half of all health facilities in the country (Kimalu *et al.,* 2004). Government funded public health facilities are organised in a pyramid structure with four levels. On the lowest level are dispensaries and medical clinics which provide the most basic services, this is followed by health centres and sub district hospitals on the level above. The third level consists of district hospitals and provincial general hospitals which provide more comprehensive services. Moi Referral and Teaching hospital in Eldoret and Kenyatta National Hospital in Nairobi are the two national hospitals which provide health care that supersedes all other facilities in the country and act as the last point of referral within the country (NCAPD & Macro, 2005).

Table 1.1: Health care providers in Kenya – a typology

Sector	Definition	Constitutes
Public	Providers funded by and in direct control of the government	• Government health care facilities • Community Owned Resource Persons
Private	Providers who fall outside the direct control of and are not funded by the government	• Not-for-profit (Mission and Non-governmental organisation) health care facilities and community owned resource persons • Private/ commercial health care facilities • **Retailers: registered pharmacies, general provision shops and mobile hawkers** • Traditional healers and herbalists

The private health sector consists of not-for-profit health care facilities and CHWs, and commercial facilities, retailers and traditional healers (Kimalu *et al.,* 2004) (Table 1.1).

The treatment seeking behaviour patterns in Kenya are such that a significant proportion of healthcare is first sought through the private sector (Chuma *et al.,* 2009; Amin *et al.,* 2003; Guyatt & Snow, 2004; Abuya *et al.,* 2007; Gitonga *et al.,* 2007). The private commercial sector in Kenya consists of health care facilities such as clinics and hospitals, and retail outlets. Private retail outlets that sell medication include both pharmacies registered with the pharmaceutical board of Kenya and others which are not registered and operate illegally. In 2004, the country was reported to have over 600 legally functioning pharmacies (HAI, 2004). Pharmacies can legally sell medicines classified by the PPB as Over the Counter (OTC), Pharmacy (P) and Prescription Only Medications (POM). It is also common to find medicines being sold in general provision shops and by mobile hawkers. Legally these outlets can only sell OTC medications however they are also known to stock and sell P and POM medications. CHWs are licensed to sell a limited range of treatments (HENNET, 2007).

1.1.3: Treatment of Malaria in Kenya

Kenya is divided into eight provinces, Central, Coast, Eastern, Nairobi, North Eastern, Nyanza, Rift Valley and Western. A study carried out in 2009 (Noor *et al.,* 2009) showed that a majority of the country falls into low transmission areas with P. *falciparum* parasite rate observed in children 2 to less than 10 years ($PfPR_{2\text{-}10}$) estimated at < 5%. Nairobi, Central, Eastern and Rift Valley provinces were estimated to have the lowest transmission rates, with $PfPR_{2\text{-}10}$ of <0.1%. Nyanza province was estimated to have the highest transmission rates with an estimated $PfPR_{2\text{-}10}$ of >=40%. Also in 2009, Kenya reported 10 million suspected cases of malaria, and over 200,000 malaria admissions. The latest data collected on malaria deaths was in 2006, when 40,000 deaths were documented to be malaria related (World Malaria Report, 2008). Although the country has seen a recent decline in observed malaria cases (O'Meara *et al.,* 2008), the numbers still remain unacceptably high.

In Kenya, CQ was the most commonly used drug to treat uncomplicated malaria cases for 50 years. CQ resistance started emerging in 1978 which later led to it being replaced with SP. Unfortunately within 2 years resistance to SP developed, forcing the country to reconsider alternative treatment options (Shretta *et al.,* 2000, Amin *et al.,* 2007). In 2004 Kenya changed its anti-malarial treatment policy to the ACT artemether-lumefantrine (AL) (Amin *et al.,* 2007). Free distribution of AL in the public sector began in mid 2006. The policy change process was to occur in phases over a five year period with the first two years seeing AL distributed through public health facilities. This would allow time for the country to develop experience before the policy could be rolled out to a wider range of providers such as private-for profit clinics and the retail sector in order to increase access (Amin *et al.,* 2007). However, progress in rolling out AL in the retail sector has remained very slow, as explained below. The then Kenya malaria treatment policy recommended presumptive treatment with AL for all febrile children under the age of 5, except those living in low risk areas such as Nairobi and Central Province. All febrile cases 5 years and above were to be parasitological diagnosed for malaria before treating with antimalarial drugs (MOH, 2001). After more than a year of distributing AL free of charge within the public sector, studies carried out in Kenya's public health facilities revealed that only 26% of children presenting with fever (a clinical symptom of malaria) in public health facilities who would benefit from this treatment were prescribed it. This was despite interventions such as in-service training and awareness campaigns implemented to promote uptake (Zurovac & Rowe, 2006). A separate study in the form of a household survey, published in 2007 evaluated treatment of malaria within the community (Gitonga *et al.,* 2007). The study was carried out in four endemic districts in Kenya and revealed that 90% of caregivers took some action to treat a child's fever within 48 hours of symptom onset. Of these, 47% first sought treatment in the private retail sector and only 35% went to public or not-for-profit health facilities. A small proportion, 23% of all these fevers were treated with an anti-malarial within 48 hours, of which 61% were obtained from the public sector, 28% from the retail sector and 10% by self administration of medicines available in the household. The proportion of febrile children who received the first line recommended AL within 48 hours was only 10%. As expected, the majority of AL (95%) was dispensed from public health facilities. A national survey had similar findings, showing 8% of children under five with fever taking AL, and 4.2% taking it on the same day or following day of fever developing (KNBS & ICF Macro, 2009), with around 70% of all ACTs being sourced from a government health facility/ worker (DOMC, 2007). More recent data from the Kenya Malaria Indicator Survey (DOMC, 2011) showed some improvements in some of the malaria case management indictors for children under five years across the country. Fever prevalence was 51%. Of those fevers 35% received an antimalarial, 18% received an ACT and 11% received this ACT on the same or next day of fever developing. Of those who had treatment sought for their fever, 23% received it from a private sector health facility or pharmacy, and 9% from a shop. Only 12% of fevers had blood samples taken for malaria testing. What this partly demonstrates is that health care for malaria is heavily sourced from the private retail sector; however, the services received remain poor. Care provided from this sector for the treatment of malaria is mainly based on ineffective medications (Amin *et al.,* 2003; Abuya *et al.,* 2007; Gitonga *et al.,* 2007). Since a high proportion of individuals seek treatment within the retail sector (Chuma *et al.,* 2009; McCombie, 1996; Williams & Jones, 2004), encouraging AL distribution within this sector at an affordable price, along with improving the quality of health care services offered has the potential to significantly expand the coverage of effective malaria treatment within the community.

More recently, in line the update World Health Organisation (WHO) malaria treatment policy (WHO, 2010), the new National Malaria Strategy which commenced in 2009 now recommends that where possible, all febrile cases should undergo diagnostic testing either with Rapid Diagnostic Tests (RDTs) or microscopy prior to treating for malaria (DOMC, 2009). To achieve this, the Division of Malaria Control (DOMC) intends to introduce RDTs in facilities without microscopy equipment, and rehabilitate the microscopy equipment present in facilities that have them available (DOMC, 2009). Data based on the more recent Kenya National Malaria Strategy released in 2009 (i.e. that all febrile patients should be tested for malaria diagnostically, if the test is positive the patient should be treated with AL, and if negative the patient should not be treated for malaria) showed that only 12% of febrile children under five, presenting at a government health facility were treated appropriately (DOMC, 2010). Weaknesses within the public sector have been acknowledged by the government who are working in collaboration with both local and international organisations to improve performance (DOMC, 2010; DOMC, 2009).

1.1.4: Improving Delivery of Antimalarials through Retailers in Kenya

HMM is a strategy that has been supported by RBM with the aim of increasing prompt and effective treatment of malaria within the community. This strategy exploits the strengths of providers outside the public facilities and improves their services. It can be delivered through retailers, CHWs or other community members, and is generally implemented alongside public health sector delivery (RBM, 2005).

Kenya can be considered a pioneer in HMM interventions targeting retailers. Training of general shopkeepers in the mid-1990s began on a pilot basis in coastal Kenya, combined with community information campaigns (Marsh *et al.,* 1994; Marsh *et al.,* 2004). This was followed by a scale up of the intervention to other parts of Kenya, which was more recently documented in Abuya *et al.,* (2009). Other interventions were piloted in the Western part of Kenya (Muturi, 2001; Tavrow *et al.,* 2003), one involving the training of retailers (Muturi, 2001) and the other involving the use of mobile and stationary wholesale vendors in educating private sector retailers, such as pharmacies and general shops, on appropriate selling of antimalarial treatment (Tavrow *et al.,* 2003), results of these pilots are reviewed in Chapter 2.

All these interventions were carried out when anti-malarial monotherapies such as SP and amodiaquine were still effective and were the first line of treatment for uncomplicated malaria. These monotherapies were affordable and readily available in retail outlets. The introduction of AL as first line treatment posed major challenges to the shopkeeper training strategy. AL was too expensive for the majority of consumers to afford (Arrow *et al.,* 2004). In addition the Kenyan Pharmacy and Poisons Board classified AL as POM, making it officially available only in healthcare facilities and pharmacies and to those prescribed it by healthcare professionals. Existing policies to train shopkeepers on the first line medicine were therefore no longer appropriate or likely to have a significant impact on coverage of appropriate treatment.

1.1.5: ACT Subsidies in the Private Sector

These challenges led to the consideration of subsidising ACT in the Kenyan private sector, and the decision to carry out the pilot described in this thesis. Two other ACT HMM pilots were implemented at the same time: the Sustainable Healthcare Enterprise Foundation (SHEF) introduced subsidised AL and RDTs in their network of Child and Family Wellness Clinics (CFW) run by trained healthcare professionals (SHEF, 2008); and the Kenya Red Cross piloted provision of AL and RDTs through CHWs (Kenya Red Cross; Beyond prevention: HMM in Kenya 2010). However, no other studies in Kenya have implemented ACT subsidies through normal drug retailers.

On an international level, similar retail subsidies were being introduced elsewhere, including Uganda, Nigeria, Tanzania, Cambodia, Madagascar and Rwanda (Schäferhoff & Yamey, 2011). Moreover, the issue has gained increasing prominence with the roll out of the Affordable Medicines Facility-malaria (AMF-m), which from 2010 has been introduced in 8 countries, including Kenya, under AMF-m Phase 1 (Schäferhoff & Yamey, 2011). The primary function of the AMF-m is to provide a "co-payment" directly to pre-selected manufacturers of ACTs in order to reduce the price to national level wholesalers to approximately $0.05. As a result of this co-payment, it is expected that the price of ACTs will be comparable to that of other less effective anti-malarial monotherapies, such as CQ and SP in the private sector, and free or low cost in the public sector, crowding out the monotherapies. The AMF-m mechanism also provides funding to countries for supporting interventions to facilitate the widespread uptake and responsible usage of ACTs by patients, targeted at wholesalers (e.g. incentives to distribute to remote areas), retailers (e.g. shopkeeper training, suggested retail prices (SRP)), and consumers (e.g. social marketing) (AMF-m, 2007).

Limited experience with private-sector ACT subsidies elsewhere indicates that they can lead to increased ACT uptake and decreased monotherapy use (Sabot *et al.,* 2009; Sabot *et al.,* 2008). However, no data are available on the impact on the key outcome of coverage of prompt effective treatment of fever at the community level. With only a subset of the community using retail outlets, it is not clear if an intervention targeting the private sector will demonstrate a significant effect on overall treatment coverage. In addition, there are concerns that shopkeepers may not stock the subsidized medicines due to capital constraints; that brief training may be insufficient to change treatment practices; and that retailers may not pass on the subsidy to the consumer, preferring instead to maximize their profits. Concern has already been raised in the Kenyan media that the subsidy is not being passed on to consumers (Nation editorial 7/2/11). Also, it is not known whether caretakers of young children will be willing to change their treatment practices and to trust shopkeepers to provide good quality ACTs, while there are also fears that the strategy will divert careseekers from trained providers. There are concerns that the subsidies will be taken advantage of by the relatively well off, with the poorest in the community unable to afford even the subsidised ACT (D'Alessandro *et al.,* 2005; Oxfam, 2009). Moreover, the increased availability of ACTs may encourage the misuse and over use of the treatment, increasing drug selection pressure, encouraging parasite resistance to the treatment (D'Alessandro *et al.,* 2005; Staedke *et al.,* 2009). Finally trying to improve ACT availability may drain resources from other useful malaria interventions in the public sector (Oxfam, 2009).

This thesis aims to address some of these research gaps in the context of the Kenyan pilot of retail sector subsidized ACT.

1.2: OBJECTIVES

1.2.1: General Objective:

To evaluate to what extent the provision of pre-packaged, subsidized, AL delivered through private sector retailers will improve the coverage of prompt effective anti-malarial treatment.

1.2.2: Specific Objectives:

1) To determine the impact on the proportion of children under five with fever being treated promptly with appropriate anti-malarial treatment, and adhering to the correct dose ***(accessibility and utilisation)***
2) To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years ***(provision)***
3) To determine distribution of benefits of retail sector delivery of AL by socio-economic status ***(equitable coverage)***
4) To explore reasons for the impact observed and identify any challenges in the implementation process ***(explanation of experience)***

1.3: ORGANISATION OF THESIS

Chapter 2: Review of literature- Home Management of Malaria

This chapter reviews the evidence on different aspects of HMM, including its definition, treatment seeking behaviour and evaluations of HMM interventions.

Chapter 3: Review of literature- Evaluating Public Health Interventions: A Review of Approaches

This chapter reviews the available evidence on the advantages and disadvantages of different study designs used to evaluate public health interventions.

Chapter 4: Study site and methodology

This chapter describes the setting in which the study took place and the intervention design. Three data collection activities took place in this study, a provider survey, a mystery shopper survey and a household survey. This chapter describes how the sample sizes were derived for each data collection activity, gives details on how the data collection activities took place and describes the data analyses used to derive outcome measures.

Chapter 5: Provider survey

Data collection for the provider survey took place by interviewing providers in retail outlets that met the selection criteria. The interviews focused on provider behaviour and practices in treating malaria. This chapter goes through baseline and follow-up results of the provider survey and discusses the findings.

Chapter 6: Mystery shopper survey

Data from this survey were collected by data collectors disguised as caregivers of a child with fever seeking help from selected providers to see what treatment and advice the latter would offer. This chapter goes through baseline and follow-up results of the mystery shopper survey findings and discusses the findings.

Chapter 7: Household survey

Data collection for the household survey activity took place by interviewing caregivers who had children suffering from fever within two weeks prior to the interview date to see what kind of actions they took in treating the child's fever. This chapter goes through the baseline and follow-up results of the household survey and discusses the findings.

Chapter 8: Discussion and Conclusion

This final chapter brings together the results from all the data collection activities to synthesise the findings and identify the implications for policy and future research. It discusses the context in which the study was conducted, the study's strengths and limitations, triangulates outcomes from the three data collection activities, and compares the study outcomes to previously available evidence. It ends with the conclusions of the PhD.

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CHAPTER 2

HOME MANAGEMENT OF MALARIA

As noted in Chapter 1, a large gap exists between the RBM target that '80% of those suffering from malaria should receive appropriate treatment within 24 hours' and current coverage. This chapter explores the factors that contribute to this gap, and reviews the evidence on the effectiveness of home management for malaria (HMM), a strategy aimed at increasing coverage of appropriate malaria treatment.

The chapter begins with an overview of the literature on treatment seeking behaviour for malaria-related illness in malaria endemic areas in general (section 2.1) and in Kenya in particular (section 2.2). Section 2.3 reviews the literature on HMM in general, while section 2.4 focuses specifically on HMM interventions in the retail sector. Since recent reviews already exist in most of these areas, the first 3 sections draw mainly from these reviews, supplemented by additional papers where necessary. However, for section 2.4 a systematic literature search was conducted as up to date reviews were not available.

2.1: OVERVIEW OF TREATMENT SEEKING BEAVIOUR FOR MALARIA; SUB SAHARAN AFRICA

2.1.1: Defining Malaria

The concept of malaria is understood differently across community members and cultures. Some community members are aware of the symptoms and transmission of malaria through mosquitoes, and acknowledge it as a distinct disease. Others may accept malaria as a distinct disease in the absence of understanding its etiology and transmission. Despite the differing ways in which malaria is defined, the most common symptom known to correspond to uncomplicated malaria is fever (McCombie, 1996; Williams & Jones, 2004; Mccombie, 2002). For example, in Ghana the word 'asra', translated as fever was closely related to malaria, in Zimbabwe 'nyongo' described symptoms of fever and headache which a large part of the population thought to be caused by mosquito bites; and in Kenya the word 'homa', used to describe fever is linked to malaria through a specific form known as 'homa ya malaria' (Agyepong, 1990; Agyepong, 1992; Vundule & Mharakurwa, 1992). The initial signs and symptoms of malaria share similar characteristics to pneumonia (O'Dempsey *et al.,* 1993), and both diseases are leading causes of morbidity and mortality in children under five in sub Saharan Africa (Black *et al.,* 2003, 2010; Kinney *et al.,* 2010). This means that there is potential for mis-diagnosis between the two diseases, resulting in the overtreatment of malaria, especially in regions where malaria cases are on the decline (Okiro *et al.,* 2009; Omera *et al.,* 2008). In addition, malaria as a disease is generally quite difficult to diagnose.

Laboratory diagnosis is rarely available in many settings, due to a lack of equipment, supplies and trained staff. Clinical diagnosis is challenging as the signs and symptoms of uncomplicated malaria include fever, headaches and chills, which overlap with the symptoms of many other diseases. As a result, over diagnosis of malaria is common (McCombie 2002). For example, in Uganda, 92% of children presenting at clinical facilities with fever were clinical diagnosed with malaria, but lab tests came out positive in only 62% of cases. In areas of low malaria prevalence, an even higher percentage of fevers are likely to be over-diagnosed (Lubanga *et al.,* 1997). It is estimated that of all clinically diagnosed malaria patients, an average of 61% (ranging between 28% and 96%) will give a negative laboratory diagnosis (Amexo *et al.,* 2004).

2.1.2: Sources of Treatment for Malaria

A review by McCombie (1996) evaluating malaria treatment practices showed that around 40 to 95% of reported malaria cases will seek some kind of treatment, with the majority of studies showing the proportion to be over 90%. Seeking treatment was more likely to occur if the patient was suffering from fever and if the illness was taking longer than usual to disappear (McCombie, 1996). Most first actions were shown to take place from a few hours of symptom onset to within two days (Williams & Jones, 2004). The number of cases that took two or more forms of actions varied from 11 to 90%, with most studies showing more than 40% of cases likely to take more than one action, but few taking more than two. The number of actions taken was shown to be linked to severity of symptoms, with more severe cases taking more actions (McCombie, 1996). The three main actions identified are self-treatment, use of the formal health care sector and seeking care from traditional healers (McCombie, 1996; McCombie, 2002; Williams & Jones, 2004).

Self-treatment can be defined as any treatment that does not involve consulting a healthcare provider or a traditional healer. This ranges from use of a cool bath to reduce fever, to administering a course of antimalarials purchased from the informal health sector such as retail outlets, itinerant vendors, and even other households. The purchasing of medications from a pharmacy is also often placed in this category even though this can be seen as accessing treatment from someone who is considered part of the formal health sector. Although there is variation between studies, it appears that the proportion of patients suffering from symptoms of malaria that self treat is high, and that a majority of these patients have purchased medication from an informal outlet such as a drug shop or general shop selling medicines (McCombie, 1996; McCombie 2002; Williams & Jones, 2004). In Zimbabwe, for example, a drug survey revealed that 43% of antimalarials used were obtained from shops (Raynal, 1985).

The formal health sector includes hospitals, clinics, and dispensaries in both the public and private sector. In some studies village health workers are included in this category. A review looking at treatment seeking behavior in malaria (McCombie, 1996) estimated that slightly over half of 'malaria' patients will visit this sector (when it includes village health workers), though this sector was usually not utilised as the first choice of treatment. For example, a study in Uganda showed that only 17% of patients had not tried any other form of treatment before visiting a clinic (Kengeya-Kayondo 1993).

Traditional healers are described in many terms including 'demon healers', 'wound healers', 'bone setters' or 'old women', who advise the community through their own knowledge and experience (Williams & Jones, 2004). They are believed to cure a range of disease that are thought to be either clinical, emotional or spiritually related. Visits made to the traditional healer by patients suffering from symptoms of 'malaria' are relatively rare, with most studies suggesting 10% or less of patients will visit one or use traditional medicines, if suffering from malaria symptoms (McCombie, 1996).

2.1.3: Factors Influencing Treatment Seeking Behaviour

Decisions on where treatment is sought are not passive but based on many factors such as treatment experience, local beliefs about how the illnesses should be treated, influence of social networks, and a realistic appraisal of available options (McCombie, 1996; McCombie, 2002; Williams & Jones, 2004). A common method of treatment seeking behavior is known as 'trial and error', 'nomadic', or 'try and see', whereas symptoms alter or treatment remains ineffective, so do the beliefs and explanations of cause and therefore treatment (Williams & Jones, 2004). Generally, for the treatment of febrile illness, the first response is self-treatment (Ryan, 1998; McCombie, 2002). As described in the 'trial and error' approach, if the initial self-treatment attempts result in no improvements, care will then generally be sought from what is perceived to be a more qualified healthcare provider. These usually include medical health care providers (from the formal private, public or Non-Governmental Organisation (NGO) sector) but sometimes traditional healers (McCombie, 2002).

It is thought that conventional medicines from drug outlets are commonly used as a first response because such outlets tend to be closer than public health facilities and, unlike public health facilities, usually have a reliable supply of drugs. Providers from these outlets are thought to be friendly and willing to offer treatment on credit if funds are not currently available. Another factor determining where treatment is sought is the severity of symptoms (McCombie 2002; Williams & Jones, 2004). Certain symptoms or combination of symptoms, for example a high or persistent fever or a combination of fever with vomiting, cough or diarrhoea, are perceived to be more serious than others, requiring advice, most often directly sourced from the formal health sector. Prevalence of certain diseases may also influence behavior. For example, in malaria endemic areas, where people are more familiar with its symptoms, self-treatment of the disease may be more common than other forms of care (McCombie, 2002). Studies have shown that traditional healers may also refer their patients to more conventional healthcare providers if the symptoms are perceived to be more amenable to conventional therapy, if physical symptoms worsen or if it seems to them that the traditional remedy has failed. It is suggested that when it comes to malaria, some healers claim not to cure malaria symptoms. Other symptoms such as convulsions have been perceived to be the specialty of a traditional healer (McCombie, 2002).

Cost is an important determining factor in treatment seeking behaviour. Incurred costs may include what is spent at the point of care, on transport to the source of care, and also in the form of time lost from productive activity. For example in Somalia, people stated that there was no reason to waste time and money on treatment for malaria if it could be cured at home with traditional remedies (Abyan & Osman, 1993). A related determinant is socio-economic status. In general poverty has been identified as a major constraint for access and use of healthcare facilities (McCombie, 1996). A study in Congo showed that those who spoke French, and were therefore viewed to be of a higher financial status were slightly less likely to treat their children's illness at home or buy the drugs in a market, suggesting a potentially higher use of health facilities (Carme *et al.,* 1992). A review carried out by Barat *et al.,* (2004) showed that richer individuals are more likely to seek treatment for malaria from both the private and public health facilities, while poorer individuals are more likely to access treatment from traditional healers. Those with a lower level of education have also been shown to access the formal health sector less, probably due to education being linked to higher SES, and those less educated being less likely to understand the seriousness of certain diseases (McCombie, 1996; Williams & Jones, 2004).

Seasonality may also affect treatment seeking behavior. In rainy seasons it may be difficult to use roads to access formal healthcare services, making one opt for self-treatment. During times of harvesting, farming demands may make it time consuming to visit facilities that are far away. Also, in times of poor crop yield, money may be saved to purchase food instead of purchasing medical treatments. In such cases, treatments may be limited to what is already available at home rather than spending money at health care facilities (Williams & Jones, 2004).

Some studies have shown age to be an important determining factor to where treatment is sought. In some cases, caregivers have been more likely to take a younger child directly to a healthcare facility rather than take chances and treat the child at home first, an action they are more willing to take with their older children (McCombie, 2002). When it comes to gender, women have been shown to experience difficulties in accessing the formal healthcare system mainly because of the locus of decision making with the household (Williams & Jones, 2004). Women may be prevented by the more 'senior' males within the household from seeking appropriate treatment. They may also not be financially empowered to access treatment if funds are controlled by their spouses. Their heavy workloads may not permit them to take time out and seek treatment, and due to social pressures they may feel constrained in expressing feelings of being ill and needing to access care (Williams & Jones, 2004).

Finally, area of residence has been shown to influence treatment seeking practices. In Nigeria, for example, home treatment was more common in rural areas, while health centre use was more common in urban areas (Odebiyi, 1992). The location of residence may be an indicator of more fundamental factors such as beliefs in different types of treatment, ease in accessing different healthcare sectors or be a reflection of socio-economic status (McCombie, 1996).

2.1.4: Quality of Care

Reviews looking at patients' quality of care have revealed poor healthcare practices within both the formal (public and private) and informal healthcare sector. Poor practices observed from both sectors include lack of counselling, poor diagnosis, rude treatment of patients and caregivers, as well as over prescription of drugs, incorrect dosing, and delays in initiation of treatment and diagnosis. Studies carried out in the formal healthcare sector have shown that despite providers being knowledgeable about malaria and its treatment, this knowledge is not always implemented (Brugha & Zwi, 1998; Ofori-Adjei & Arhinful, 1996; Williams & Jones, 2004). One of the reasons given for this is that prescribers are often influenced by demands from the community (Ofori-Adjei & Arhinful, 1996; Williams & Jones, 2004). In the informal health sector, the situation is often worse since many practicing have insufficient pharmaceutical or healthcare training. This has led to studies observing drugs being sold that are not recommended by national guidelines, inappropriate dosages being recommended, poor if any advice given to patients, and poor storage and labeling of medications (Williams & Jones, 2004). Apart from the lack of knowledge and clinical skills, and client demand, poor quality of care in the informal sector has been thought to be attributed to the influence of pressure from pharmaceutical companies trying to increase market share in order to maximize profits, and ineffective local regulation (Williams & Jones, 2004; Goodman *et al.,* 2007).

The quality of care is also determined by poor patient adherence. Inappropriate drug dosages and incorrect timing between doses are frequently observed (Williams & Jones, 2004; McCombie, 1996). Despite being given the correct administration advice, patients may not follow this advice at home. In Kenya for example, 55% of those seen at a health centre did not follow dosing instructions (Mwenesi *et al.,* 1995). A 2005 review looking at adherence in the community to CQ, which also has a 3 day regimen, showed only a median of one third using it correctly (Yeung & White, 2005). Other studies on ACT adherence have shown varying results, ranging from 39% to 90% (Depoortere *et al.,* 2004; Beer *et al.,* 2009; Fogg *et al.,* 2004; Kachur *et al.,* 2004; Piola *et al.,* 2005). Predictors of adherence have been shown to include the level of education, receiving the correct number of tablets (Beer *et al.,* 2009) and counselling practices (Kachur *et al.,* 2004).

The most common practices seen in poor adherence is failure to complete full courses of treatment. This has been observed in both the formal and informal sector (McCombie, 1996). It has been observed that patients tend to stop taking medication when they feel better and save the tablets for later (McCombie, 1996). A review carried out by Yeung & White (2005) concludes that adherence to antimalarial treatment is affected by patients not having access to affordable treatment or not receiving the correct advice on how the treatment should be administered. The review highlights that patients seem to be adherent to treatments known to be effective than those that are less efficacious (Yeung & White, 2005).

2.2: OVERVIEW OF TREATMENT SEEKING BEHAVIOUR FOR MALARIA; KENYA

A review looking at treatment seeking behaviour in Kenya reports similar outcomes to reviews carried out across SSA (Chuma *et al.,* 2009; Chuma *et al.,* 2010). The review showed a majority of patients with fever would take some kind of action to treat their fever with up to 25% of fevers left to resolve without any action taken (Chuma *et al.,* 2009). Most of the time only one type of action would be taken (Chuma *et al.,* 2009; Chuma *et al.,* 2010). This was demonstrated in Gucha and Kisumu districts where 87% and 75% of all fevers respectively were treated with only one action (Guyatt & Snow, 2004; Ruebush *et al.,* 1995). As seen in other SSA counties, self-treatment with OTC medication was the first most common form of care sought, with care sought from the formal health sector being much less common (Chuma *et al.,* 2009). In one study, close to half of all fevers experienced in children under five were treated with drugs brought from either a shop or a chemist. Only one third reported accessing treatment from a public health facility (Chuma *et al.,* 2010). Treatment was not usually sought immediately on the onset of symptoms; rather a median of 2 days delay was observed (Chuma *et al.,* 2009; Chuma *et al.,* 2010). Patients were more likely to wait longer than 2 days to seek treatment from the formal health sector (Chuma *et al.,* 2009).

The review showed that variability exists across the country in the proportion of fevers being treated with an anti-malarial, with results ranging from 23% to 91% (Chuma *et al.,* 2009). Fevers were more likely to be treated with the government recommended antimalarial from the formal health sector compared to the informal sector, and were more likely to be treated with an antipyretic from the informal sector (Chuma *et al.,* 2009). This has been demonstrated in a cross-sectional study carried out by Gitonga *et al.,* (2007) soon after the policy change to AL as the first line treatment for uncomplicated malaria. The study showed that of the 31% of resolved fevers, 10% received AL of which 95% was sourced from the formal health sector (Gitonga *et al.,* 2007).

The factors determining patterns of treatment seeking behaviour in Kenya remain similar to those identified in other SSA countries described above. A key factor identified is community members' perceptions of the quality of care received from government health facilities and effectiveness of treatments offered (Chuma *et al.,* 2009; Chuma *et al.,* 2010). In a focus group discussion (FGD), members claimed the government sector was staffed with young health care workers with inadequate training and disrespectful behaviour, deterring them from this sector (Chuma *et al.,* 2010).

Issues regarding quality of care received from both the informal and formal sector also remain similar to those observed in other SSA countries. The uptake of the policy change to AL in Kenya has been slow in all sectors, with ineffective anti-malarial monotherapies still being prescribed, as shown in the study carried out by Gitonga *et al.,* (2007) and described above. Studies have identified several factors that may have contributed to this poor uptake. These include poor supply chains which result in frequent stockouts, and prescribers being cautious in prescribing AL, fearing stock outs if the drug is prescribed to all deserving cases; ineffective monotherapies still being supplied to government health facilities; health care staff shortages, combined with high workloads and poor follow-up supervision and training; unclear treatment guidelines and contradictory training messages that confused health workers (Wasunna *et al.,* 2008; Kangwana *et al.,* 2009). It is argued that better regulatory enforcement of the policy change, education of the public on malaria treatment with awareness of ineffective treatments, and buy-in from pharmaceutical companies on the policy changes may have helped improve the quality of care received for the treatment of malaria in all health care sectors (Chuma *et al.,* 2009).

Patient adherence is also seen as a problem in Kenya (Chuma *et al.,* 2009; Chuma *et al.,* 2010). Poor adherence has been blamed on complex drug regimens that are difficult to follow, and inconvenient drug timings that are difficult to follow especially for mothers who leave their children at home to go work on the farms or look for casual work (Chuma *et al.,* 2010).

The above reviews demonstrate some of the key challenges faced in malaria treatment in both Kenya and the rest of SSA. These challenges affect care givers, providers and the government. In summary, challenges affecting caregivers include being equipped with the knowledge in identifying malaria and knowing where to seek effective treatment. Caregivers also need to be able to overcome the physical barriers in seeking effective treatment such as cost of treatment and distance to treatment outlets. Challenges affecting providers include making accurate diagnoses, knowing how to treat malaria patients effectively and creating the appropriate environment to be able to put that knowledge into practice. Governments face challenges in creating an enabling environment to allow successful implementation of their malaria policies. This includes providing training to providers, rolling out community awareness campaigns to inform consumers on effective malaria treatment, ensuring sufficient supplies of antimalarial medications at government facilities and monitoring all sectors providing health care to ensure adherence to policy guidelines. I now turn to a strategy aimed at addressing some of these challenges.

2.3: HOME MANAGEMENT OF MALARIA

HMM was designed to overcome barriers to accessing effective malaria treatment and improve quality of care received, by working with both the formal and informal services offered within communities, outside of clinical settings. HMM is designed to enable caregivers to recognise malaria illnesses early and respond appropriately; to ensure that targeted health care providers have adequate knowledge and capacity to respond to malaria illness; and to create an environment that enables successful implementation of the strategy. In order to achieve these objectives it is argued that an HMM strategy should have an effective communication strategy, should train community based service providers on the skills and knowledge necessary to delivery adequate healthcare, and should guarantee sufficient supplies of effective high quality, pre-packaged anti-malarial medication at the community level. Monitoring and evaluation of all these activities and their impact is also necessary to ensure effective implementation of the strategy (RBM 2005).

The RBM has integrated HMM as part of its strategy to improve malaria treatment especially for non-immune individuals at risk of malaria, primarily children under five residing in high malaria transmission areas. Others who may benefit from HMM are people residing in low to moderate malaria transmission areas who may be exposed to malaria epidemics. This strategy is designed to provide care in areas that are inadequately served by the public healthcare system, augmenting rather than replacing public healthcare (RBM, 2005).

2.3.1: Current Evidence on HMM

A review on HMM was carried out by Hopkins *et al.,* (2007), specifically to evaluate the health impact of community- and home-based treatment for malaria in Africa. Studies were included in the review if they used antimalarial treatments to presumptively treat for fever and if the treatment was administered by local community members with no formal healthcare education. The outcomes monitored were specific health care indicators such as malaria morbidity or mortality, malariometric indices including parasite rates, haemoglobin or packed cell volume (PVC). A total of six studies were identified and evaluated, one in Kenya, The Gambia, The Democratic Republic of Congo, Ethiopia and two in Burkina Faso.

Five of the studies implemented HMM interventions through community healthcare workers (CHW) and one directly targeted caregivers. Only one study carried out in Ethiopia was able to show significant changes in mortality. This was a randomised controlled trial carried out in a rural seasonal malaria transmission area, where 24 clusters of villages with the highest malaria morbidity were paired by their under 5 mortality rates. Within each pair one was assigned into the intervention arm and the other the control arm. The intervention involved educating mothers to recognise symptoms of malaria in their sick children and treat with CQ promptly. Free CQ was distributed to all households through mother coordinators and it was up to the mothers to replenish supplies when need be. The results showed a significant reduction ($p < 0.003$) in under five mortality rate of 40.6% (95% CI 29.2 – 50.6) in the intervention arm compared to the control arm (Kidane & Morrow, 2000).

Four studies were able to demonstrate some improvements in malaria morbidity or malariometric indices, but not mortality. In Burkina Faso for example, a study compared outcomes of morbidity in children who received the intervention compared to those who did not receive it. The study was carried out in an area with hyper-endemic seasonal malaria. The intervention involved training of CHWs and a group of mostly older mothers on aspects of malaria. Health centre staff were trained to package age specific CQ treatment doses with aspirin and sell them to the CHWs, who in turn would sell them to local mothers requiring treatment for their child, at a price that would create some profit, and therefore creating an incentive to continue selling. The outcomes of the study showed a significant reduction in the progression to severe malaria between children who received prompt treatment (within 24 hours) with pre-packaged CQ compared to those who did not receive the treatment (risk ratio 0.47, 95% CI 0.37 – 0.60; $p < 0.0001$) (Sirima *et al.,* 2003).

One study in Kenya observed no significant change in any of the outcome indicators measured. The study was conducted in the hyper to holo-endemic malaria area near Lake Victoria, comparing two community intervention areas to one control area. Households within the communities were interviewed at six to nine month intervals on births, deaths and migration. In addition two biannual surveys were conducted in randomly selected villages to assess parasitaemia and antimalarial antibodies. The intervention involved training CHWs to give CQ free of charge for the presumptive treatment of fever, and to refer any serious cases. The study showed high usage of CHWs, however the presumptive treatment with CQ was found to have no impact on malaria specific or overall mortality, nor was a change seen in the parasite prevalence or serological markers. The low impact of the intervention was thought to be as a result of the high use of CQ prior to the study (Spencer *et al.,* 1987a; Spencer *et al.,* 1987b).

The authors of the review concluded that a more robust meta-analysis could not be conducted due to the heterogeneity of the study designs and outcome measures. The evidence available on the effect of HMM on health outcomes was considered to be limited since only a total of six studies were identified, of which only one was able to show any benefits on mortality as an endpoint. The authors were therefore left with a list of unanswered questions, such as what is the optimal HMM intervention, would programme outcomes be similar in different settings such as rural versus urban, what are the safety risks in delivering treatment in this manner, and are HMM interventions sustainable and cost effective? They suggested that these questions could only be addressed through further studies (Hopkins *et al.,* 2007).

Another review evaluated the effects of differing types of interventions on provider practice and user behaviour, in order to improve prompt treatment practices for children under five suffering from fever. In this review providers were defined as those responsible for dispensing antimalarials and were further categorized as public and private; formal, and informal or community-based (Smith (b) *et al.,* 2009). This review also looked at interventions targeting users, such as caregivers. Most interventions targeting this group focused on health education messages or the use of pre-packaged drugs with pictorial or verbal instruction. The trial designs were either randomised controlled trials, time series measurement, pre-post with or without a control group or post design with a control. The studies had to have reported on at least one RBM- Monitoring and Evaluation Reference Group indicator (RBM-MERG), with numerators and denominators presented (Smith (b) *et al.,* 2009). The main findings are summarised below. The examples used here are limited to the non-clinical setting as this is the target area for HMM interventions. The examples in this section exclude studies on interventions targeting private informal providers (drug vendors, chemical sellers and regulated or unregulated general shopkeepers that stock and sell medicines) as these are discussed in more detail in section 2.4.

Only one study in Uganda (Nsungwa-Sabiiti *et al.,* 2007) looked at the key RBM outcome of 'prompt and effective treatment'. The intervention was developed into a national strategy and involved recruiting and training community drug distributors, who had the role of treating presumptive fevers in children with pre-packed CQ-SP (known as Homapak®). Mothers were also educated on appropriate treatment practices. The intervention resulted in a significant (P=0.01) 14% point increase in effective treatment in the intervention group, when compared to the control.

The majority of studies not monitoring promptness but looking more generally at effective treatment (defined as the combination of receiving the correct antimalarial at the correct dose and for the correct duration) showed improvements in this outcome measure. For example, an intervention in Mali involved the training of informal providers in the community, also known as village drug kit managers. They were trained on appropriate presumptive treatment of fevers, while the rest of the community was exposed to sensitization and education activities in order to increase their demand for services offered by the managers. The intervention improved provider treatment behaviour by 11% points ($P=0.042$) when compared to a control where providers only received basic training. Adherence to treatment in the intervention group was also greater by 41% points when compared to the control group ($p<0.001$) (Winch *et al.,* 2003). One study in Ghana showed that training teachers to treat fever presumptively and supplying them with pre-packed malaria treatment resulted in 8% point increase in children in the intervention group receiving correct treatment compared to the control arm ($P<0.001$), however, no significant difference was observed in adherence ($P=0.94$) (Afenyadu *et al.,* 2005).

Studies that looked at individual components of effective treatment on their own (either receiving the correct treatment, dose or number of doses) showed varied outcomes. Three studies carried out in The Gambia, Cameroon and Zambia, evaluating interventions designed to educate carers on malaria treatment showed significant increases ($P<0.001$) in their knowledge of the correct anti-malarial treatment and doses required (Kaona & Tuba, 2003, Nkuo *et al.,* 2005; Menon *et al.,* 1988). Another study in Burkina Faso (Pagnoni *et al.,* 1997) used community based mother educators to educate women to actively seek the correct treatment for their children, while making pre-packaged treatment available through CHWs. The results showed significant improvements ($P<0.0001$) in the use of the correct antimalarial, the correct dose and for the correct duration. However, in Kenya, when behaviour was assessed in an intervention involving education of mothers, no significant difference between the groups was observed when it came to using the correct dose (Tavrow & Rennie, 2004).

The authors of the review conclude that an HMM model based on training CHWs on presumptive treatment and providing them with pre-packaged antimalarials to distribute, as well as having community awareness activities is the most common HMM model, which tends to lead to statistically significant but modest improvements in treatment behaviour. The authors suggest that the addition of supervision and provision of incentives to this model may further improve behavioural practices. The authors felt that pre-packaging of anti-malarial treatment was one of the most effective ways of increasing adherence. Similar to the previous review (Hopkins *et al.,* 2007), the authors' main concerns regarding the studies include the scarcity of high quality evaluations that allow for concrete conclusions to be made on the effectiveness of interventions; the short periods between implementation of the intervention and their evaluation do not allow one to judge the sustainability of the observed outcomes; and finally most studies were implemented on a local level, meaning that the impact of interventions at a national level remains unknown (Smith (b) *et al.,* 2009).

2.4: HMM INTERVENTIONS IN THE PRIVATE RETAIL SECTOR

2.4.1: Evaluation of HMM Interventions Targeting the Private Retail Sector

This thesis evaluates the impact of a specific HMM intervention on the proportion of children under five, with fever, receiving appropriate anti-malarial treatment. The HMM intervention targets providers within the private retail sector, and includes training and providing subsidised effective antimalarial treatment through these outlets, combined with community awareness activities educating caregivers on appropriate malaria treatment practices. This section reviews current evidence of the effects of HMM interventions in the private retail sector. A PubMed search was carried out using the 'PICO' search strategy (population, intervention, comparison and outcomes) (Higgins & Green, 2011) and the terms such as the following, for each category:

- Population: specialised drug stores, pharmacies, shop, mobile hawkers, kiosk, retail outlet, sub Saharan Africa (MeSH) (this group reflects the targeted population in the thesis);

- Intervention: home management of malaria, training, information education communication, community awareness, subsidy, social marketing;
- Control: not applicable;
- Outcome: coverage, access, counseling, dispensing, adherence, knowledge, behaviour, cost (these indicators were selected to correspond to those evaluated in chapters 5-7 of the thesis to allow for comparison).

A separate search was carried out for each category, each term in these searches was separated by 'OR'. Then all categories were combined using 'AND'. The search was limited to sub Saharan Africa due to the distinctive nature of the retail pharmaceutical sector in these areas; all literature was restricted to the English language. An initial search was carried out in December 2010 and updated in July 2011. A further search was carried out in the grey literature under Google scholar, and also through discussion with experts in the field. In addition, previous reviews carried out on similar topics were sourced and used to identify additional studies (Goodman *et al.,* 2007; Abuya *et al.,* 2009; Smith (a) 2009; Smith (b) *et al.,* 2009; Wafula & Goodman, 2010; Patuoillard *et al.,* 2007, Hopkins *et al.,* 2007). Relevant studies from these reviews were then accessed through websites, through contacting authors and through work colleagues. No limit was placed on the date of the study.

Search outcome: A total of 21 reports were identified as evaluating HMM strategies in the private retail sector. 10 were published in peer reviewed journals, the rest were reports in the grey literature. The reports constituted 22 HMM evaluation studies. Six studies were from Kenya, five from Nigeria, three from Uganda, three from Tanzania, and one each from Cambodia, Zambia, Ghana, Madagascar and Senegal. Although the study was limited to sub Saharan Africa, a study in Cambodia was included as it formed one of only four studies (three of which were based in sub Saharan Africa) that evaluated the impact of ACT subsidies on HMM and provided some very useful findings. The components of

HMM intervention strategies evaluated varied and included provider training, franchising of trained outlets, supervision of trained outlets, provision of pre-packaged drugs, provision of cheaper anti-antimalarial treatment either through pooled procurement or through the use of subsidises, and community awareness activities (Table 2.1). Each intervention consisted of one or more of these components (Table 2.1). Methodologies in study design varied. Only one study was planned as a probability design having a cluster randomised controlled approach; most studies were plausibility or adequacy designs, with only one being initially designed as a randomised controlled trial however ended up as a plausibility design. The years in which the reports came out ranged from 1992 to 2010. Data collection activities included quantitative (such as retail audits, provider survey interviews and mystery shopper surveys) and qualitative methods, with studies using one or more of these techniques. This review will focus on the quantitative outputs from the results.

The effect of subsidies on the cost of antimalarial treatment: Four studies looked at how interventions involving subsidised ACTs were able to control costs of these antimalarials at the retail level. Two studies were successful in showing their intervention having the desired effect on the cost of the drugs. One was a study carried out in the rural parts of Tanzania where AL was highly subsidised and distributed through the normal supply chains to drug stores known as '*duka la dawa baridi*'. This led to the mean price being paid for ACTs for children under five years of age ($0.35) being significantly lower than less efficacious antimalarials SP ($0.51) and amodiaquine ($0.30). This study also showed that having a suggested retail price (SRP) artificially inflated AL prices, above those that would have been determined by the market, implying that SRPs should be used with caution until their impact on pricing is better understood (Sabot *et al.,* 2009). In Senegal the government launched the distribution of subsidized artesunate+amodiaquine through private pharmacies where artesunate+amodiaquine was assigned a SRP to match that of the public sector. The intervention looked to be successful as a pricing survey showed private outlet prices of the antimalarial to be similar to those in the public sector (Sabot *et al.,* 2008). In Kenya, an intervention carried out by the Sustainable Healthcare Enterprising Foundation (SHEF) that was supposed to supply free AL through trained and franchised CFW retail outlets found that more than half of patients interviewed paid for their antimalarial (Sabot *et al.,* 2008). In Cambodia, the NGO Population Services International (PSI) supplied pre-packaged ACT to wholesalers, who were recommended to sell their antimalarials to retail outlets at a subsidised price of $0.55. However, retail outlets ended up paying an average price of $0.75 per adult dose and $0.69 per child dose. This was 36% and 25% points higher, respectively than the recommended price (Sabot *et al.,* 2008).

Caregivers' knowledge: Two studies looked at the effect of education of caregivers on their knowledge of malaria. In Zambia a study carried out in Nakonde district in the Northern Province by Kaona & Tuba (2003) evaluated an intervention informing mothers of issues relating to malaria through trained village health motivators and vendors. The intervention increased caregivers' ability to identify symptoms of simple and complicated malaria in their child by 1.32 and 1.51 times respectively. The same caregivers were also more likely to know the correct dose of the recommended antimalarial (CQ) to give their child. The study in Cambodia, where subsidised pre-packaged ACT was distributed through wholesalers to the private retail sector, also showed a 22% point increase in caregivers' awareness of the recommended malaria treatment after a parallel mass media campaign was run promoting the subsidised treatment (artesunate+mefloquine) (Sabot *et al.,* 2008). All results on caregivers' knowledge were descriptive, it is therefore not known if the changes observed were statistically significant.

Provider knowledge: Seven studies carried out across three countries, Kenya, Nigeria and Tanzania, evaluated the effect of training retail providers on their knowledge of malaria.

The studies covered different aspects of malaria. Two studies evaluated more general knowledge of malaria, including diagnosis, treatment and prevention. One of these studies, based in the Igbo-Ora town of Western Nigeria (Oshiname & Brieger, 1992) showed that a 5 day training session significantly improved general knowledge of malaria by 29% points. Another study based in Bungoma district, Kenya (Tavrow *et al.,* 2003), which involved 5 days training of trainers of wholesale suppliers improved by 16% points the general knowledge of retail outlet providers, who had been trained by the wholesalers. Three studies evaluated the effect of their interventions training on knowledge of signs and symptoms of malaria. The greatest improvement of knowledge was observed in an HMM study in Nigeria carried out by the Society for Family Health (SFH)/ PSI (Gilpin *et al.,* 2006) in Abia State, which showed a 36% point increase after 1 day of training. The smallest improvement was observed in a separate study carried out also in Abia state, Nigeria, prior to the SFH/ PSI study, where a 17% point increase was documented also after 1 day of training (Greer *et al.,* 2004). A study that was carried out by the NGO Merlin in the Kisii and Gucha districts of Kenya showed an increase of knowledge of 27% points after 2 days of training (Muturi, 2001). Four studies evaluated the effect of training on providers' knowledge on the correct treatment and dose for malaria in differing age groups. Three of these studies were in Kenya, one was the study in Bungoma district showing a significant 33% point increase after 5 days of training (the recommended treatment in this intervention was SP) (Tavrow *et al.,* 2003), another was the Merlin study that showed a significant 9% point increase after 2 days of training (with SP being the recommended treatment) (Muturi, 2001). A further Kenyan study carried out in three districts Kwale, Makueni and Busia, with differing malaria transmission rates showed that providers in the intervention group were significantly ($P<0.001$) more knowledgeable about the correct treatment and dose of the recommended antimalarial treatment (amodiaquine) after 2 days of training compared to those with no training (Abuya *et al.,* 2009). A study in Kibaha district, Tanzania, showed a significant 45% point improvement in knowledge of the correct dose of SP for a 2 year old child after only one hour of one on one training, though the sample size was very small (N = 18 respondents) (Nsimba, 2006).

Provider behaviour: Four studies reported on the advice that staff gave on how to administer antimalarials purchased from their outlets. All these studies had some component of provider training or negotiation sessions in their HMM strategy. Two studies, both carried out at the coast of Kenya were able to show outlets targeted with the intervention giving statistically significantly more advice than those left to function as normal. These studies were related, with the first being designed as a small scale pilot study, which was followed by the second larger scale implementation study. The small scale pilot study, involving 3 days of training, direct observation, supply of work aids and refresher training of providers showed a difference of up to 96% points giving advice on anti-malarial treatment, however it was not specified whether this advice was appropriate or not (N = 99 & 119 respondents at baseline and follow-up respectively) (Marsh *et al.,* 1999). The larger scale intervention demonstrated an increase of 86% points, with more intervention outlets giving appropriate advice on recommended antimalarials (CQ or SP) dispensed after 4 days of training with a refresher course, accompanied with biannual monitoring (N = 299 & 224 respondents at baseline and follow-up respectively) (Marsh *et al.,* 2004). The Kenyan study that evaluated an intervention in Kwale, Makueni and Busia districts, involving 2 days of training resulted in a 26% point increase in providers recommending the correct antimalarial (SP or amodiaquine) with the correct advice (Abuya *et al.,* 2009). Other studies looked at similar interventions in Nigeria and Uganda (Greer *et al.,* 2004). The Ugandan study in Luwero district, involving 3 days of education, negotiation and persuasion training, combined with mentoring and supervision showed a significant 58% point increase in providers explaining to customers how to administer medication (CQ combined with SP) in cases of simple malaria (N = 57 & 66 respondents at baseline and follow-up respectively). However a 9% point ($p>0.05$) decrease was observed in providers giving similar advice in complicated cases of malaria. The study in Abia state, Nigeria, which combined a one day training with supply of pre-packaged treatment (SP packaged separately to CQ), led to an 18% point significant increase in advice given on recommended malaria treatment.

When it came to discussing malaria danger signs with customers purchasing antimalarials, only the one study in Bungoma district in Kenya, involving the training of wholesalers to inform their retail counterparts, as well as provision of job aids and monitoring, showed a statistically significant difference of 20% points in intervention outlets (Tavrow *et al.,* 2003). Three studies showed increases ranging from 30-42% points. These were the small scale coast study in Kenya, the Ugandan study in Luwero district and the Tanzania study in Kibaha district. All these studies had training as a large component of their HMM intervention (Marsh *et al.,* 2004; Twafik *et al.,* 2006; Nsimba, 2007). The study in Abia state, Nigeria with training and pre-packaged treatment showed an insignificant 5% point decrease in providers informing customers on danger signs, but in Uganda negotiation sessions, monitoring and supervision support led to a 34% point significant increase in the same (Greer *et al.,* 2004).

Three studies looked at the influence of the intervention on the availability of recommended antimalarials found in targeted outlets compared to those not exposed to the intervention. These studies were the Kenyan study where subsidised AL was made available in CFW outlets, the Nigeria study in Abia state (Greer *et al.,* 2004) and the study based in rural parts of Tanzania where subsidised treatments were made available to the private sector outlets '*duka a dawa baridi*' (Sabot *et al.,* 2009). Both the Kenyan and Tanzanian study reported significant increases in outlets stocking the recommended antimalarial (Sabot *et al.,* 2009). In Tanzania, the provision of heavily subsidised AL using the normal distribution chain led to a significant 72% point increase in stocks of the antimalarial in the target outlets (N = 133 & 151 at baseline and follow-up respectively). In the Kenyan study, the distribution of free AL to the franchised CFW outlets led to a 39%

point increase in availability of the antimalarial in the outlets (Sabot *et al.,* 2008). The study in Nigeria involving the introduction of age specific, pre-packaged antimalarial (CQ packaged separately to SP) together with provider training led to a large increase of 88% points in availability of the treatment in retail outlets, which is likely to be a significant improvement although no hypothesis testing was carried out (N = 147 & 204 at baseline and follow-up respectively) (Greer *et al.,* 2004).

Adequacy of treatment received for malaria symptoms and patient adherence: Eight studies evaluated the effect of the intervention on adequacy of antimalarial treatment received and patient adherence. Four studies were in Kenya, two in Tanzania and one in in Uganda and in Nigeria. Of the three Kenya studies, one was the small scale study based at the coast which showed that training of shopkeepers and distribution of job aids led to a significant 50% point increase of caregivers purchasing any antimalarial treatment to treat their child's fever, and a significant 58% point increase in caregivers purchasing an adequate dose of the recommended antimalarial (CQ) at follow-up compared to baseline (N = 289 & 150 at baseline and follow-up respectively) (Marsh *et al.,* 1999). The same study was able to show a significant 71% point increase from baseline to follow-up in caregivers administering adequate doses of the antimalarial to their child (N = 109 & 108 at baseline and follow-up respectively) (Marsh *et al.,* 1999). The larger scale study at the coast showed that training of providers increased the percentage of childhood fevers being treated with any anti-malarial by 37% points, at one of the follow-up time points. An increase was also observed in the percentage of shop treated fevers receiving adequate doses of the recommended treatment (SP) by 29% points (Marsh *et al.,* 2004). The Kenyan study in Bungoma district which involved training of mobile and stationary wholesalers, who were to train retailers and distribute job aids and consumer awareness posters resulted in a significant 15% point increase in shoppers purchasing an adequate drug (SP) and dose for their malaria symptoms (Tavrow *et al.,* 2003). In one of the Nigerian studies based in

Abia state, the intervention involving training of providers, pre-packaged antimalarial (CQ and SP in separate packages), and community awareness activities led to significant 39 and 33% point increases in patients receiving the correct dose for simple and complicated malaria, respectively and a 44% point increase in the percentage of private medicine vendors recommending or giving the correct dose of antimalarial. The same report evaluated a similar study in Luwero district, Uganda that showed training through an education, negotiation and persuasion method (this involved critically evaluating current practices and using this as a point for negotiating changes to improve practice), with monitoring and support resulted in large significant 71% and 88% point increase of providers recommending the correct medication (CQ and SP combined) for simple and complicated malaria respectively, and 68% point increase in recommending the correct dose of that treatment (Greer *et al.,* 2004; Twafik *et al.,* 2006). Another study in Zambia, Nakonde district showed 60% more children were likely to receive the correct dose of the antimalarial (CQ) after drug vendors and village health motivators were trained on malaria and its treatment (Kaona & Tuba, 2003).

Table 2.1: Summary of studies evaluating HMM strategies in the private retail sector

No.	Report/ Publication	Country	Study design	Target group	Intervention
1	Gilpin *et al.,* (2006), Improving management of malaria among patent medicine vendors in Lagos, Kano and Abia states, Nigeria	Nigeria (Lagos, Kano and Abia states)	Before and after	-Patent Medicine Vendors (PMV)	-Advocacy visit to state ministries of health and executives of State PMVs association -One day training of PMVs -National radio generic ACT promotion
2	Brieger & Ogunlade (2001), Lessons learned and impacts of the CPH Experience in Nigeria. Arlington, Va: BASICS II for the United States Agency for International Development.	Nigeria	Control and intervention arms	-Community based organizations (CBOs) -Private health care facilities	-Training particularly on malarial prevention
3	Oshiname & Brieger (1992), Primary care training for patent medicine vendors in rural Nigeria	Nigeria (Igbo-Ora town)	Baseline and follow-up with intervention and control arms	-PMVs -Wholesalers -Consumers	-Design and production of a shopkeeper job aid -Design and production of a client awareness aid -2, 3 hour orientation sessions for wholesale owners -Training and equipping of mobile vendors (entrepreneurs who purchase drugs from wholesale general shops (not wholesale pharmacies) and re-sell them by motorcycle or bicycle to small retailers, and wholesale counter attendants (wholesale counter attendants are stationary employees of wholesale pharmacies or general shops who are paid a daily wage) -5, 1 day training sessions
4	Brieger *et al.,* (2002), Promoting prepackaged drugs for prompt and appropriate treatment of febrile illnesses in rural Nigerian communities	Nigeria (Oyo, Abia and Enugu states)	Baseline and follow-up	-Variety of distributors including village health workers, patent medicine vendors and health clinic staff -Mothers	-Prepackaging of chloroquine and cotrimoxazole provided in blister packs with colours and small pictures to denote the two main age groups of 6-11months and 1-6years -Training of village health workers, PMVs and health clinical staff -Training of mothers as community health educators -Sales strategy: recruiting a variety of distributors who were trained to perform individual and village health education; general community level promotional activities. Educational aid was a pamphlet describing malaria and the need for prompt action and a story flipchart

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Table 2.1 continued

No.	Report/ Publication	Country	Study design	Target group	Intervention
5	Greer *et al.*, (2004), Improving Management of Childhood Malaria in Nigeria and Uganda by Improving Practices of Patent Medicine Vendors	Nigeria (Abia state)	Before and after	-PMVs	-PMV training consisted of a one-day, focused session on key practices to improve management of simple and complicated malaria. -The introduction of pre-packaged, age-specific CQ and SP -A comprehensive social marketing and behaviour change communication strategy, which included mass media to promote new pre-packaged antimalarials (PPAMs) and the PMVs who displayed shop identifiers from the training
		Uganda (Luwero district)	Before and after	-PMVs	- Advocacy and partnerships - Selection and training of moderators - Negotiation sessions; three-day negotiation training - Monitoring and support supervision
6	Tawfik *et al.*, (2006), Negotiating improved case management of childhood illness with formal and informal private practitioners in Uganda	Uganda (See Greer *et al.*, 2004)	(See Greer *et al.*, 2004)	-(See Greer *et al.*, 2004)	-(See Greer *et al.*, 2004)
7	The CORE Group, Minnesota International Health Volunteers (2004), Improving malaria case management in Ugandan communities: Lessons from the field	Uganda	Before and after	-Drug vendors -Community volunteers	-Training of drug vendors and other community volunteers. Drug vendors were trained initially for 3 days followed by a subsequent 1 to 2 day training which took place every 3 to 4 months. -Provision of job aids -Drug vendors (and others) encouraged to form self-governing professional association to ensure the sustainability of the project -Malaria awareness days -Distribution of malaria calendars with information -FGDs to address misconceptions specific to the community
8	Talisuna *et al.*, (2009), Cost if killing patients: subsidizing effective antimalarials	Uganda	Baseline and follow-up with control and intervention arms	-Licensed and unlicensed drug shops	-Availability of subsidies ACTs -Supportive interventions that included information education and communication, and training of providers

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Table 2.1 continued

No.	Report/ Publication	Country	Study design	Target group	Intervention
9	Kaona & Tuba (2003) Improving ability to identify malaria and correctly use chloroquine in children at household level in Nakonde District, Northern Province of Zambia	Zambia (Nakonde district)	Baseline and follow-up with control and intervention arms	-Village health motivators (VHM) -Vendors	-A total of 27 VHMs from each intervention village attended a seven-day course, which focused on general knowledge of malaria: cause, prevention, treatment using national malaria treatment guidelines and referral of severe cases to health centres -The VHMs were provided with a VHM manual for reference, in case they forgot some basic facts -VHMs made house-to house visits once a week, informing mothers and other caretakers about both correct administration of chloroquine and identification of malaria in under-five children. VHMs encouraged mothers to obtain treatment guides each time they bought chloroquine from a vendor. Any child suffering from suspected malaria was immediately referred to the rural health centre. They took records of children who complained of fever and recorded any deaths that occurred in each household within their villages.
10	Mensah, (2005), The Licensed Chemical Sellers' Franchise model: CAREshops in Ghana. Accra, Ghana	Ghana	Stepped wedge approach	-Licensed chemical sellers	-Implementation of an innovative franchise programme called CAREshop -Sellers selected and trained, outlets are remodelled and branded, pooled procurement of drugs delivered directly to the retailer, retailers and supervised and provided with management support
11	Tavrow *et al.,* (2003), Vendor-to-vendor education to improve malaria treatment by private drug outlets in Bungoma District, Kenya	Kenya (Bungoma district)	Control and intervention	-Private drug outlets -Wholesalers -Consumers	-Design and production of a shopkeeper job aid -A client awareness aid -Orientation of wholesale owners-2, 3hr orientation sessions -training and equipping of mobile vendors (entrepreneurs who purchase drugs from wholesale general shops (not wholesale pharmacies) and re-sell them by motorcycle or bicycle to small retailers) and wholesale counter attendants (wholesale counter attendants are stationary employees of wholesale pharmacies or general shops who are paid a daily wage) -5, 1 day training sessions

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Table 2.1 continued

No.	Report/ Publication	Country	Study design	Target group	Intervention
12	Marsh *et al.,* (1999), Changing home treatment of childhood fevers by training shop keepers in rural Kenya	Kenya (Coast)	Before and after	-Shopkeepers	-Three day training of shopkeepers -1-2 hours of individual training sessions in outlets for direct observation -Supply of work aids -2 day refresher training after 6 months
13	Marsh *et al.,* (2004), Improving malaria home treatment by training drug retailers in rural Kenya	Kenya (Coast)	Stepped wedge approach, comparing early and late phase and before and after	-All drug retailers selling AM or AP -Late phase: outlets selected by popularity, geographic access and the perceived stability of outlets and trustworthiness of the owners and their employees	-Work shop training over 4 days; 1 day refresher training -Accreditation posters pasted on outlets -Outlets visited twice annually by community worker trainers to monitor activities -Community information activities
14	Muturi, (2001), Lessons Learned in Training Retail Sellers on Correct Use of OTC Antimalaria Drugs in Kenya	Kenya (Kisii and Gucha district)	Baseline and follow-up	-Shopkeepers	-2 day training of shopkeepers -Shopkeepers provided with job aids -Demand generation through IEC campaigns -Quality assurance: shopkeepers only promote drugs recommended and approved by the MOH. Regular supervision carried out by the local ministry of health staff and Merlin (an NGO) staff -Spot checks were done and on the job training conducted -Supportive supervision carried out and discussions held with shopkeepers on areas needing strengthening -Refresher training conducted based on supervision findings
15	Abuya *et al.,* (2009), Impact of Ministry of Health Interventions on Private Medicine Retailer Knowledge and Practiced on Anti-Malarial Treatment in Kenya	Kenya (Busia, Makueni and Kwale district)	Control and intervention (originally planned as a cluster randomised controlled trial)	-Private medicine retailers	-Trainers and co-trainers trained PMRs in 2-day workshops at local venues. The training covered signs of simple and severe malaria; malaria treatment and prevention; drug resistance; referral practices; storage and expiry of medicines and communication skills. -Public information activities were based on local public meetings and use of posters outside trained outlets and in public places.

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Table 2.1 continued

No.	Report/ Publication	Country	Study design	Target group	Intervention
16	The Sustainable Healthcare Enterprise Foundation (SHEF) (2008), Evaluating the introduction of Artemether Lumefantrine into selected clinics operating under CFW franchising system in kirinyaga,embu & mbeere districts	Kenya (Kirinyaga, Embu and Mbere districts)	Baseline and follow-up	-SHEF healthcare providers	-Issuance of messages on malaria morbidity, mortality, diagnosis using RDT as well as training the SHEF healthcare providers. SHEF also provided subsidised RDT and AL to the 10 clinics. -6 community focus group discussions and 13 key informant interviews with health care givers. Quantitative data collection was by response to a semi-structured questionnaire, exit interviews and desk research that involved retrieval of Daily Patient Register records from SHEF clinics
17	Population Services International (PSI) (2006), PaluStop Pre-Packaged Treatment for Simple Malaria in Children under Five in Madagascar.	Madagascar	Baseline and follow-up	-Doctor prescribers, -Pharmacists wholesalers -Retailers	-Supply of two pre-packaged treatment kits for uncomplicated malaria -Subsidizes the consumer price to just $0.03 -Series of TV and radio spots, a song and video clip, and educational film for *PaluStop*. Each of these were developed and pre-tested among target groups through focus groups discussions or interviews
18	Nsimba, (2007), Assessing the impact of educational intervention for improving management of malaria and other childhood illnesses in Kibaha district-Tanzania	Tanzania (Kibaha district)	Intervention and control arms	-Drug sellers/ dispensers	-One on one training session lasting for one hour -Posters provided to both arms as dispensing aides -Individual information provided to the intervention arm
19	Health Research for Action (2006) Review of the accredited drug dispensing outlets (ADDO) roll out programme in Tanzania	Tanzania (Ruvuma region)	Baseline and follow-up	- Small drug shops also known as *duka la dawa baridi* permitted to sell OTC medicines, but not POMs (general stores not targeted)	-Dispenser training courses of 40-day duration - Mandatory training courses for owners of 5-day duration - applications for opening an accredited outlet was required to assess if the proposed location was within specified guidelines -Incentives for participation included provision of business training and facilitation of loans for required improvement of shops, allowances to sell selected Part I drugs on prescription
20	Sabot *et al.,* (2009) Piloting the Global Subsidy: The Impact of Subsidized Artemisinin-Based Combination Therapies Distributed through Private Drug Shops in Rural Tanzania	Tanzania (Maswa, Kongwa and Shinyanga rural districts)	Control and intervention	- Small drug shops also known as *duka la dawa baridi* permitted to sell OTC medicines, but not POMs (general stores not targeted)	-Distribution of ACTs at highly subsidised prices (Supply chain: Norvartis-project managers-wholesaler-drug shops) -One day training of shop attendants -Behavioural change communication activities including local radio adverts, wall paintings and cultural shows.

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Table 2.1 continued

No.	Report/ Publication	Country	Study design	Target group	Intervention
21	Sabot et al., (2009), Distribution of Artemisinin-Based Combination Therapies through Private-Sector Channels *Lessons from Four Country*	Kenya (See SHEF, 2008)	(See SHEF, 2008)	-(See SHEF, 2008)	-(See SHEF, 2008)
		Senegal	Cross sectional	-Private pharmacies	-Distribution of subsidized artesunate+amodiaquine through private pharmacies - artesunate+amodiaquine was assigned a suggested retail price to match that of the public sector
		Cambodia	Combination of surveys carried out before and after the study	-Sales representatives -Wholesalers -Private providers	-Blister-packaging, and marketing of Malarine and Malacheck -PSI-trained sales representatives directly distributed the products to a network of wholesalers in 17 out of 20 malaria endemic provinces - PSI also trained private providers on appropriate diagnosis and treatment as well as on communication and education through mobile video unit shows, mass media, and special events, among others
		Tanzania (See Sabot *et al.*, 2009)	(See Sabot *et al.*, 2009)	-(See Sabot *et al.*, 2009)	-(See Sabot *et al.*, 2009)

Only two studies looked at the impact of distributing subsidised ACT on adequacy of treatment received and patient adherence. The Kenyan study that involved community awareness activities and training of health care workers in the franchised CFW drug outlets, together with the provision to patients of subsidised AL after confirmation by an RDT (patients had to pay \$0.65 for a consultation and RDT). The intervention resulted in no significant difference between the percentage of children adhering to the recommended malaria treatment (AL), when compared to government health facilities. The intervention also had no significant effect on the proportion of patients who took effective anti-malarial treatment on the same or next day after development of malaria symptoms (Sabot *et al.,* 2008; SHEF 2008). The study however did show that between the two provider types, 19% point increase in children from the trained outlets received the recommended treatment according to their weight (which is the recommended method of dosing for that drug) (Sabot *et al.,* 2008). In rural Tanzania, the HMM strategy that involved the provision of heavily subsidised treatment (AL) sold to a wholesaler and supplied to small drug shops '*duka la dawa baridi'* through the normal supply chains. The AL was pre-packaged with simple dosing instructions in the local dialect (Kiswahili). The intervention was evaluated across three study areas (districts). One area remained as a control, another area had subsidised AL supplied to the '*duka la dawa baridi'* outlets using existing supply chains, and the third area also was supplied with subsidised AL but it had a SRP marked onto the packaging. The intervention areas supplied with AL also had supporting interventions such as a one day training of attendants in the '*duka la dawa baridi'* outlets, regulatory strengthening to promote effective distribution of the treatment, and Information, Education and Communication (IEC) campaigns such as radio adverts and cultural shows. Data were collected at five different time points, one at baseline and the other four during the first year of implementation. The study showed that subsiding

AL led to a significant 53% point increase in shoppers being offered it at the drug outlet (Sabot *et al.,* 2009).

Discussion: The HMM retail interventions evaluated have covered a wide range of strategies and antimalarials. Nearly all showed improvements in their outcome indicators. Most interventions included training of either providers or users as part of their HMM intervention, however there was no obvious correlation between the length of training and success of the intervention. It was difficult to assess the quality of training and its impact on outcomes as very few studies used training as the sole component of the HMM intervention. Most combined training with other supporting activities such as the provision of job aids, follow-up monitoring and provision of pre-packaged anti-malarial treatment with pictorials demonstrating administration. Other studies have observed that training of providers alone does not have much effect on practice of malaria treatment (Zurovac *et al.,* 2008; Wasunna *et al*., 2010; Osterholt *et al.,* 2006; Rowe *et al.,* 2000; Rowe *et al.,* 2003). Some reasons for these observations include a narrow approach to training that uses a didactic approach without considering wider determinants of practice such as patient demand and traditions and values of the society from which the providers originate from (Chandler *et al.,* 2008; Rowe (b) 2005). Possible ways of improving the impact of training on practice include ensuring that the training is of a high standard; making the training sessions more interactive; increasing health worker morale to encourage them to implement and maintain the taught methods of practice (Gouws *et al.,* 2004), provision of supporting material at the provider's place of work such as job aids (Zurovac *et al.,* 2004; Ross-Degnan *et al.,* 1997) and following on from training having onsite refresher training and a good level of supervision post training to ensure training practices are maintained (Ofori-Adjei & Arhinful, 1996; Rowe (b) *et al.,* 2005).

It is also difficult to make any further general conclusions on HMM interventions in the retail sector from this review. Studies differed in the study design, data analysis techniques used and the type of outcome measures used. The interventions implemented were also varied, with few if any studies having exactly the same strategy. Many of the interventions incorporated more than one component, for example training of providers may be included with community awareness programmes or the provision of subsidised pre-packaged antimalarial treatment. Few studies carried out hypothesis testing on their outcome results so it is difficult to interpret the importance of any observed differences. All these factors make comparability across studies difficult. Furthermore, there are limitations in interpreting data from the individual studies due to certain weaknesses in the study designs. Some studies had very small sample sizes. Only one study planned its study design as a cluster randomised approach, however in the end, due to the way in which the intervention was implemented, randomisation of it into control and intervention areas was not possible. Most studies did not even include a control group, relying instead on pre and post data only. This may have exposed studies to possible confounders. Very few studies have been published in peer reviewed journals, thus the quality of the data available may also be questionable.

A review carried out by Goodman *et al.,* (2007) evaluated interventions designed to improve malaria practice of medicine sellers (commercial retailers supplying fever/malaria drugs, except formal pharmacies that are required to be staffed by a qualified pharmacist) in sub- Saharan Africa. Most of the studies mentioned in the Goodman review have been included in the above review. The review concluded that medicine sellers were willing to take part in studies and similar to the above, most studies did report improvement in the outcome measures monitored, in particular providers' knowledge and performance. Since medicine sellers were already active within communities, there was minimal requirement to invest in any further infrastructure to allow for the implementation of the interventions. This improved the cost-effectiveness of the interventions, however significant costs were still incurred in other aspects of the interventions such as training. Although the studies provided insufficient evidence to determine which interventions were most successful, certain recommendations were made: that prior to planning an intervention, carrying out a comprehensive situation analysis is important in understanding the environment and tailoring a suitable strategy; interventions are more likely to be successful if there is broad buy-in from all key stakeholders, and that to enhance sustainability of the intervention and its outcomes the intervention needs to be implemented as a continuous processes combined with supervision (Goodman *et al.,* 2007). Limitations to making further conclusions and recommendations remained similar to those mentioned in the above.

Another review (Schaferhoff & Yamey, 2011) evaluated how private sector subsidies on ACTs affect their price, market share, availability and use. The review looked at four sub-national pilots and six national programs. All, apart from one sub-national study in Angola have been included in the above review. The HMM intervention evaluated in this thesis was also included. The review also looked at six national programs, one in Senegal and one in Cambodia, which have also been discussed in the above review under 'The effect of subsidies on the cost of antimalarial treatment'. Other national programmes included were in Cameroon, the Democratic Republic of Congo, Madagascar and Rwanda. The review concluded that private sector subsidies have shown to reduce consumer prices, increase ACT market share by crowding out monotherapies, however are unlikely to benefit the poorer in society. The reviewers acknowledged weakness across the study designs such as most studies not being randomised, others not having a control group or baseline data. These factors mean that bias and confounding may have not been controlled for, therefore limiting the reliability of the data.

In all these reviews, it is notable that only four studies reported on interventions involving ACT, one in Kenya, Tanzania, Cambodia and Senegal (Sabot *et al.,* 2008). There is also one study in Uganda that showed ACT subsidies led to their increased availability in drug shops, however data on this study are yet to be published in full (Talisuna *et al.,* 2009). In 2007, Rwanda also introduced subsided ACTs into pharmacies, but similarly there are no published findings. A report indicates that 18 months later 80-90% of pharmacies stocked ACTs from a baseline level of 10%, and there had been large falls in the availability of other antimalarials such as SP, CQ and artemisinin monotherapies, thought to be due to significant government engagement in ensuring the successful implementation of their antimalarial treatment policy (Schaferhoff & Yamey, 2011). Data on Rwanda is also yet to be published. As AMF-m roll out only began in late 2010, no evaluations are yet available on this strategy. Similar to all the other HMM studies, of the existing studies focusing on ACTs, variation exists between them on the design of the HMM intervention, including the use of different distribution systems, the way the subsidy was implemented, and the supportive interventions used to promote uptake of the programme's antimalarial. There is also variation in the study designs and outcomes evaluated. These variations make it difficult to collate the data and make any broad conclusions. Limitations also exist within studies, for example, in Cambodia, no formal evaluations took place and no baseline survey was undertaken, instead the results of the intervention were drawn from a number of different studies with different study methodologies, so it is hard to know the true effects of the intervention. In both Kenya and Senegal, the studies were of a small scale making it difficult to generalise the study findings to other settings or to a larger scale. In Kenya, only a small number of specially trained and supported outlets were used to distribute the programme's antimalarial. These outlets are only available in a small area of the country, limiting the impact of the intervention if it was scaled up. Also, none of these studies address the key RBM indicator of access to prompt effective treatment. Further research is required to address these issues (Sabot *et al.,* 2008).

Three other reviews have looked at the effects of interventions in the retail sector on a wider range of diseases such as acute respiratory infections, diarrhoeal diseases, and sexually transmitted infections (Smith, 2009; Wafula & Goodman, 2010; Patouillard *et al.,* 2007). Their main conclusions were that although there are a wide number of innovative schemes to improve care in this sector, training of providers remained the most popular. Also, like the above reviews, most interventions tended to show some form of improvement in the outcome measures. All reviews raised similar concerns as those mentioned above. These include the limited number of studies falling into the selection criteria, the lack of rigour in study design including the few studies reporting data on how well the interventions were able to target different socio economic groups, and the relatively short follow-up periods making it difficult to gauge long term effectiveness of the interventions (Smith, 2009; Wafula & Goodman, 2010; Patouillard *et al.,* 2007).

2.5: CONCLUSION

Much is known about treatment seeking patterns and the reasons for these, and evidence has shown that quality of care for malaria is poor in both public and private sectors. HMM was proposed to address this, but the evidence base remains patchy. Many studies show that such interventions can impact provider knowledge, and some show changes in provider behavior and patient adherence. However, only one retail sector study has looked at the impact on coverage of prompt effective treatment. Only one study carried out in Ethiopia, involving CHWs has shown an impact on mortality. None of these studies involve the use of ACT. They therefore stem from a very different era when recommended antimalarials were relatively cheap, meaning that interventions mainly focused on training and communication. In the current ACT era, widespread uptake requires antimalarial subsidies as well, yet the evidence in this area is particularly limited. This evidence gap urgently needs to be addressed to inform the roll out of AMF-m and other HMM strategies.

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CHAPTER 3

EVALUATING PUBLIC HEALTH INTERVENTIONS: A REVIEW OF APPROACHES

This review looks at the evaluation process in assessing public health interventions. It starts off in section 3.1 with a description of evaluation and public health interventions. This is followed in section 3.2 by a description of the methodology used for this review. Section 3.3 and 3.4 consider first steps in selecting a study design and indicators respectively. In section 3.5 the review then discusses the available evidence on 3 key classes of study designs: randomised controlled trials, plausibility, and adequacy studies. Within each class the strengths and weaknesses of the designs are discussed as well as ways to try to overcome some of the design weaknesses. The chapter ends with a brief review of more recent methods that can be used in evaluation of public health interventions.

3.1: INTRODUCTION

Evaluation can be described as the process of carrying out a systematic investigation through the collection of data (CDC, 1999). Public health interventions are programmes that are implemented with the intention of protecting and preventing ill health. They may range from direct service interventions, training and educational services, to community mobilization efforts and communication campaigns. Unlike clinical interventions which predominantly focus on targeting individuals, public health interventions tend to be oriented more towards whole communities or populations (Rychetnik *et al.,* 2002).

Evaluation is said to have four main purposes. It can be used to gain insight into innovative approaches of practice. It can also be used to review what an intervention has achieved and help decision makers describe, improve and fine tune the intervention in order to enhance its quality, effectiveness and efficiency. The results of an evaluation can be used as a catalyst to influence stakeholders to supplement the intervention or to empower participants, by increasing their sense of control of the direction of an intervention. Evaluation can also examine the relationship between the programme's activities and observed consequences (CDC, 1999; Quigley & Taylor 2004; Moore *et al.,* 2011).

Evaluation of public health interventions can be seen as a process made up of many components organized into a cyclical progression. The different stages of the cycle include engaging of stakeholders; describing to stakeholders the intervention including its mission and objectives; deciding on the appropriate study design; programme implementers implementing the intervention and evaluators implementing the study design to collect credible evidence; evaluators then come up with conclusions justified by the evidence and share any lessons to be learned (CDC, 1999). Although it is easy to portray this cycle as a neat progression from one action to the next, applying this in the real world may be very difficult.

The purpose of this review is to discuss how to best evaluate public health interventions, focusing on the stage of deciding the appropriate study design. There has been a lot of debate on choice of design, with views divided into two broad camps (though many analysts see merits in the arguments on both sides). On one side of the argument are those who support the use of randomised controlled trials (RCTs), which are considered by some as the gold standard in scientific research, providing high internal validity, significantly reducing chance, bias or confounding, and therefore viewed as providing high quality evidence for decision makers. On the other side are those that argue that despite their advantages, RCTs are often inappropriate, impossible or unnecessarily resource-intensive for evaluating public health interventions, and they also exhibit poor external validity or generalisability. They argue that the context of where a public health intervention is implemented significantly affects its outcomes, therefore designs used in evaluating them need to take this into consideration. Some claim that RCTs' lack of external validity means that one cannot determine the influences of external factors on the outcome of an intervention, something that plausibility and adequacy studies are better at doing. This review explores the strengths and weaknesses of these three main designs used in evaluating public health interventions: RCTs, plausibility evaluations and adequacy studies.

3.2: METHODOLOGY

A PubMed search was carried out using the 'PICO' search strategy (population, intervention, comparison and outcomes) (Higgins & Green, 2011) and the following terms, for:

- Population: sub Saharan Africa (MeSH);
- Intervention: public health interventions or programs;
- Comparison: randomised controlled, probability, pragmatic, quasi-experimental, plausible, adequacy or observation;
- Outcomes: positive, negative, limitations, feasibility, cost, effectiveness or efficacy.

From the papers retrieved, references were scanned for any further relevant papers. In addition, publications including grey literature were sourced from colleagues. All literature was in the English language, no limits were placed on date of publication. An initial search was carried out in December 2008, and updated in January and June 2011. A total of 33 papers and reports considered to have a direct relevance to this review.

3.3: FIRST STEPS TO SELECTING A STUDY DESIGN

Engaging stakeholders is recommended as the first step in the evaluation cycle and in many cases is considered important in deciding the appropriate study design. Stakeholders should represent groups of people and/ or organizations that have some investment or interest in what will be learned from the process and what will be done with the knowledge. They can be engaged in a variety of ways including participation in meetings and communication through reports. Stakeholders may play a role in promoting the evaluation's credibility, enhancing cultural competence, protecting human subjects and avoiding real and perceived conflicts of interest (CDC, 1999).

Three groups that may be considered as stakeholders are those involved in the intervention's operation, those served or affected by the programme and primary users of the intervention. A group of stakeholders that includes staff, funding bodies and external partners, may bring a range of perspectives or agendas for the intervention. It is important to include those involved in the intervention's operation as lessons learned from the evaluation may cause changes in the intervention and it is therefore important that they participate in this process from the beginning. Including participants who play a role in the intervention's operation will also make them feel part of the evaluation process and less like they are being evaluated or judged which may create some ill feelings (CDC, 1999). Those served or affected by the programme and primary users of the intervention should be made aware of the intervention, its goals and objectives. Their thoughts and opinions on what changes are needed and how they can be achieved may add to the evaluation's recommendations. It is also suggested that the needs and perspectives of the primary users of the evaluation be taken into consideration (CDC, 1999). Both antagonistic and sceptical group representatives should be involved as they can play a role in strengthening the evaluation's credibility. Stakeholder meetings should bring up questions regarding the intervention, one main purpose of an evaluation being to provide answers to these questions (CDC, 1999; Habicht *et al.,* 1999).

An example of groups to involve can be taken from the multi country evaluation of the Integrated Management of Childhood Illnesses (IMCI) (Bryce *et al.,* 2004). IMCI is a strategy developed to improve child health and development, and has been implemented in over 80 countries. The evaluation of IMCI took place in three countries and focused on its effectiveness, cost and impact. Stakeholders involved in the discussions of the evaluation included the evaluators, ministries of health and staff of the WHO, UNICEF, and bilateral agencies supporting IMCI implementation in the chosen study sites at country, regional and headquarters level. The stakeholders were responsible for making decisions in planning the evaluation, selecting study sites and investigators, commenting on the study design and instruments, reviewing preliminary data and formation of recommendations. Involving all these bodies was thought to increase the likelihood of the results being relevant to the needs of the programme decision makers and, that the results and recommendations would be understood, accepted, and acted on (Bryce *et al.,* 2004).

3.4: INDICATORS

Indicators translate questions or issues regarding the intervention into specific variables that can be measured; they therefore address criteria that will be used to judge the intervention. Usually multiple indicators will be needed to evaluate different aspects of an intervention (CDC, 1999). A range of frameworks have been suggested for grouping indicators into categories, each category representing a separate level of the intervention. To give an idea of the different frameworks, two are discussed below: 'process, impact and outcome' (Quigley *et al.,* 2003) and 'provision, utilization, coverage and impact' (Habicht *et al.,* 1999).

Evaluation indicators can be split into process, impact and outcome. The process of an intervention looks at how the intervention was undertaken and is important as it can be responsible for the intervention's successes or failures. Quigely *et al.,* (2003) give examples of questions that can be transformed into process indicators, these include 'how were key stakeholders identified and involved in the key stages throughout the process?', 'what time and resources were spent by individuals on specific stages of the process?' and 'how and when were recommendations delivered to the relevant decision makers?'. Impact indicators address questions on the intermediate and short-term outcomes achieved by the intervention, they include such questions as 'were the aims and objectives of the intervention achieved?' or 'how and when were recommendations for the intervention considered, accepted and implemented by the decision makers?'. Outcome indicators look at the more long term effects of the intervention for example changes on the overall health of the population (Quigely *et al.,* 2003).

A slightly more elaborate framework has been presented by Habicht *et al.,* (1999). According to them, indicators used to evaluate an intervention can be divided into four main categories, namely provision, utilization, coverage and impact. Provision looks at the services that have been provided, made available and accessible to the target population. Questions on provision may include 'are the services of the programme available?' or 'is the quality of care offered adequate?'. The indicators for the following can translate to 'what number of health facilities are offering the intervention's services per 100,000 population?' and 'what proportion of health staff have received recent training on the services that should be delivered?'.

Utilization looks at how the population accepts the services and makes use of them. A common question on utilization is 'are the services being used?', the indicator for this could be 'what number of patients presenting at the health facility receive the intervention?'.

Coverage is determined by utilization and looks at the coverage of the intervention in a given population. Coverage is described as the interface between service delivery (the managerial process) and the population (the epidemiological picture). A question in this category can be 'is the targeted population being reached?', and the indicator for this question may measure the proportion of the targeted population that received the intervention.

Finally, the intervention's influences on behaviour or health can be measured through impact. Alternatively, results from the other categories may indicate what the impact of the project is likely to be. Questions on impact ask whether the aims of the intervention were achieved. In the case of a diarrheal disease control programme, an impact indicator could look at 'time trends in diarrheal deaths and hospital admission' (Habicht *et al.,* 1999).

3.5: STUDY DESIGNS

Once indicators have been categorized, it is easier to decide which study design to use in measuring each of the categories. This section will discuss the most common study designs used in evaluating interventions, their advantages and disadvantages.

3.5.1: Randomised Controlled Trial

A randomised controlled trial (RCT), also known as a probability design, evaluates the effects of an intervention by randomly assigning the intervention into groups or individuals and comparing outcomes to controls that have not received the intervention. The randomisation process acts to ensure that all characteristics within the control and intervention arms are similar and so any differences seen between groups can be directly attributed to the intervention. RCTs are therefore often described as the gold standard design in academic research because they minimise influences of chance, confounding or bias seen compared to other study designs (Habicht *et al.,* 1999; Vandenbroucke, 2008; Victora *et al.,* 2004; Atkins, 2007).

It is argued that there are instances in the evaluation of public health interventions where RCTs may be considered unnecessary, inappropriate or even impossible to implement (Black, 1999). The key concerns centre around poor external validity, blinding, ethics, resources required including allowing sufficient time for planning, political influence, beliefs and preferences, spillover effects and difficulties in measuring rare outcomes.

As previously mentioned, a good quality RCT is considered to have high levels of internal validity, where differences identified between randomised groups can be attributed, with a high level of confidence, directly to the intervention being tested (Eldridge *et al.,* 2008).

To allow for this, RCTs require the study population and environment to be controlled in such a way as to eliminate any other influences that may affect the outcome, apart from the intervention (Habicht *et al.,* 1999). What RCTs may gain in internal validity they therefore lose in external validity, or generalisability, where the stringencies of such a design provide information on the intervention disregarding the context in which it is placed. In reality, there are likely to be external factors that may affect the intervention-outcome association. These external factors are commonly referred to as effect modifiers. Two types of effect modifiers are possible: 1) behavioural effect modification affects the actual dose of the intervention delivered to the target population. The dose of the intervention that reaches the population is dependent on the behaviours of the institution it is delivered through, the provider and recipient. Table 3.1 shows the different ways in which an intervention is implemented and how this will affect the dose of the intervention delivered and received by the target population. The study types are all RCTs, but range from clinical efficacy trials to programme effectiveness studies. In clinical efficacy trials maximum effort is used to ensure the exact dose reaches and is taken up by the recipients. This is done through a variety of strategies including intensive training and supervision of those delivering the dose, and facilitating recipients in receiving the dose through for example re-imbursement of travel costs to the point of delivery. Having to apply such unrealistically tight controls to a trial makes the design more suitable in evaluating efficacy outcomes, which aim to show whether an intervention can produce the desired outcomes under ideal conditions (Habicht *et al.,* 1999, Vandenbroucke, 2008; Victora *et al.,* 2004). A step below clinical trial studies is the public health programme, efficacy studies where no extensive efforts are made to ensure recipients receive the intervention or comply with how it should be administered. However the presence of an evaluation team and participation into the trial is argued to encourage 'best practice' where health workers may try to perform better than usual and managers may try to improve the routine running of the healthcare system. The other extreme to clinical efficacy studies is public health programme effectiveness studies, where no intervention whatsoever is used to promote delivery of the intervention or compliance to the intervention's requirements. Instead these factors are left to be influenced by the 'routine' external influences such as poor health worker performance and drug shortages. It is argued that this last type of study is extremely rare, since the knowledge of being involved in a study will have some influence on behaviour (Table 3.1), (Victora *et al.,* 2004).

Table 3.1: Different types of studies aimed at evaluating the impact of an intervention, with emphasis on the dose of the intervention that reaches programme recipients

Type of Study	**Units of Treatment**	**Delivery Mechanism of Intervention**	**Compliance with intervention by recipients**	**Example**
A: Clinical efficacy trial	Individuals	Ideal	Ideal	Classical clinical trial of drugs, vaccines, etc.
B: Public health regimen efficacy	Clusters of individuals	Ideal	Ideal	Same as above, but delivered to clusters rather than individuals
C: Public health delivery efficacy	Clusters of individuals	Ideal	Best practice	Ideal delivery is ensured, and compliance is actively promoted according to best practice
D: Public health programme efficacy	Clusters of individuals	Best practice	Best practice	Randomised allocation of geographical areas to best practice implementation
E: Public health programme effectiveness	Clusters of individuals	Routine	Routine	Randomised allocation of geographic areas to routine implementation

Source: Victora *et al.,* (2004)

2) Biological effect modification affects the dose- response association between the intervention and the outcome (Victora *et al.,* 2004). RCTs tend to exclude subjects at high risk of harms such as the elderly or children, those on multiple medications or with multiple conditions. This selection process may be very restrictive, only representing a small sub-sample of a typical real life population, therefore even after a RCT, the effects of placing the intervention on a random population may still remain unknown (Black, 1996; Atkins, 2007). If the selection criterion is very limiting then the population and therefore the outcomes seen in the trial may not be reflective of what would be seen if the intervention was implemented in a

wider community. Table 3.2 gives examples of different categories of biological effect modification.

Table 3.2: Types of biological effect modification affecting the generalisability of findings from randomised controlled trials

Category of Effect Modification	Example
A: Presence of other factors reduced the dose-response slope (antagonism)	Iron and zinc supplementation will be less effective in places where the local diet contains substances that reduce their absorption (e.g. phytates and polyphenols)
B: Presence of other factor increases the dose-response slope (synergism)	Iron supplementation will be more effective if the local diet is rich in meat and ascorbic acid which will enhance absorption.
C: Curvilinear dose-response association	Iron supplementation will have different effects on haemoglobin according to baseline iron stores. Also, iron absorption is inversely related to iron status.
D: Limited scope for improvement in the impact (outcome) indicator because other interventions already provide protection	Use of insecticide-treated bed nets will have a limited effect on malaria mortality if case-management is already appropriate
E: Intervention is inappropriate because a critical cofactor is missing	Improving water quality will have an impact on diarrheal diseases only if water quantity is adequate
F: Intervention is addressing a determinant that is not important	Energy supplementation in pregnancy will have limited impact on low birth weight if the latter is mostly due to maternal smoking and to preterm deliveries caused by infections.

Source: Victora *et al.,* (2004)

Usually in RCTs, the dose delivered, compliance to the designed intervention, and recipient population in a study will be different to that seen in real life situations. It is therefore important to provide detailed information on all these factors to allow results to be interpreted accurately (Victora *et al.,* 2004; Atkins, 2007).

Blinding of recipients and providers is an important way to reduce bias in RCTs, and lack of blinding is considered to be a serious source of potential bias (Eldridge *et al.,* 2008). However, blinding in public health interventions is not always feasible (Black, 1996; Atkins, 2007). To give an example, a clinical trial testing the efficacy of a medication may blind recipients and providers by providing placebos that look similar to the real medication. Blinding in such cases is often easy to do and is commonly done. However, a public health intervention may involve community awareness messages distributed through mass media, aimed at changing health seeking behaviour practices. In such a case both participants and providers know which communities have received the intervention and which ones have not (Stephenson *et al.,* 1998).

The ethics of carrying out an evaluation may make it inappropriate to use an RCT. If it is known that an intervention does work and is needed in a certain community it may be unethical to withhold it from those who need it, purely for the purposes of evaluation. For example, non-randomised studies have provided strong evidence for the efficacy of condoms in preventing HIV. Given the seriousness of HIV, it could be argued to be unethical to carry out an RCT that restricts condom use to the control population just to see if the outcomes would be similar to those in the non-randomised studies (Stephenson *et al.,* 1998). A possible way around this problem is that an RCT may be able to take place if resources are not enough to cover the population in need. In such situations, randomisation may be justified until enough resources can be provided for the whole community (Victora *et al.,* 2004; Black, 1996).

RCTs may also not be possible to implement because of lack of prior planning. Decisions on whether to evaluate an intervention and how to do so should be made before the intervention is implemented, preferably while implementation plans are being made since the type of study design may influence how the intervention should be implemented. This is particularly important for RCT designs since deciding how to randomise the study population into groups, then randomly allocating participants into the intervention and control requires sufficient time and planning (Habicht *et al.,* 1999; Sanson-Fisher *et al.,* 2007). RCTs should therefore at least be designed during the planning of the intervention's implementation. For many interventions, the evaluation is often thought of towards the end of the cycle, even after its implementation, making an RCT design hard to implement (Habicht *et al.,* 1999).

Difficulties may also be experienced in the randomisation process. Interventions associated with the delivery of resources and positive health outcomes may be desirable campaigning tools. Politicians may want to influence and direct the delivery of the intervention to their voters making it hard for it to be implemented in a randomised manner. It may not be advisable to override the opinions of politicians since without their support or approval the intervention may not be able to take place. As a way around this, evaluation can take place in a 'stepped wedge design' where the intervention is introduced in a random fashion but coverage increases over time to eventually include all eligible communities or populations (Moore *et al.,* 2011; Bonell *et al.,* 2011). If this option is not possible then other methods of analysis will need to be considered. Other similar problems arise in situations where changes in legislation are required or a national policy must be developed to support the intervention, and these processes may be either slow or even halt the evaluation (Habicht *et al.,* 1999; Mills *et al.,* 2008; Black, 1996). Acceptance of the intervention, not just by authoritative bodies, but also by the providers and receivers is important in allowing for better evaluation. Understanding the beliefs and preferences of participants and therefore improving the community's support of the intervention and evaluation before implementing the study is a way of ensuring that participants consent to the arm they have been randomised to. This can be achieved by involving key representatives in the stakeholders meetings if possible from the beginning (mentioned above) (Atkins, 2007).

Another factor which may be out of the control of the evaluators is that of contamination or spillover of the intervention outside of the intervention arm (Black, 1996; Sanson-Fisher *et al.,* 2007). It may sometimes be difficult to contain the resources supplied by the intervention within its allocated communities and stop significant pilferage into the control communities. For example, if the intervention involved the provision of mosquito nets to certain communities, it may be hard to stop the nets leaking into the control communities, especially if nets are perceived to have a beneficial effect on health. Where large scale pilferage is unavoidable it may be worth considering another design as the true effects of the intervention may not be reflected accurately through an RCT (Black, 1996).

It is difficult to evaluate rare outcomes in RCTs as they would require large sample sizes that may not be attainable. This is typical in post marketing surveillance of pharmaceuticals where an evaluation of rare adverse events usually takes the form of observational studies. An example of why to avoid RCTs in such situations can be taken from the drug benoxaprofen (Oparen®). Despite clinical trials in over 3000 patients, the drug had to be withdrawn after 2 years of being released due to serious adverse events and 61 deaths. These serious adverse events had not been picked up in the clinical trials as the events were rare and were not shown in the smaller groups studied (Black, 1996). Finally, when it comes to resources, RCTs are known to be costly and resource intensive, requiring evaluators with the necessary skills (Stoltzfus *et al.,* 2002; Sanson-Fisher *et al.,* 2007). A rigorous RCT cannot take place if the required finances, expertise and other resource are not made available to support the process (Stoltzfus *et al.,* 2002).

Given the factors mentioned above, it would probably be inappropriate to use an RCT design if there is insufficient time and resources to plan and implement the design properly, if the ethics of restricting the intervention to a particular group are questionable, if blinding is necessary to evaluate outcomes but not practical to implement, and if the outcomes are very rare and therefore huge numbers may need to be recruited. RCTs will probably be impossible to implement if consent or approval for the study cannot be gained from politicians, especially where legislation requires amendment to legally roll out the intervention and, if it is not possible to contain the intervention in the designated areas, making spillover a likely bias. Despite the limitations mentioned, there are times when RCTs are essential in the evaluation of public health interventions. RCTs are thought to be best placed for determining with the greatest confidence possible whether the intervention can produce the desired outcomes without the influence of external factors, therefore in evaluating the efficacy of an intervention (Habicht *et al.,* 1999; Sommer *et al.,* 1986).

3.5.1.1: RCTS: Dealing with Limitations

Due to the complex nature of many public health interventions, it may not be possible to randomly allocate individuals to receiving the intervention or acting as a control. An alternative method of randomisation is the cluster randomised trials, where randomisation occurs in blocks consisting of groups of individuals, with some groups falling into the intervention arm and receiving the intervention and others into the control (Bowater *et al.,* 2009; Craig *et al.,* 2008).

Other methods of randomisation include the randomised stepped wedge design (also mentioned above). Here randomisation takes place according to who or which group should receive the intervention and at what time. This process of evaluation is useful in situations where there are restrictions on who can receive the intervention at certain time points. Preference trials can be used in situations where patients have very strong preferences as to whether they would like to receive the intervention or not. For example, those with strong preferences are put in their preferred arm, those without strong preferences are randomised. Any imbalances in potential confounders between the arms can then be controlled for in the analysis. The N-of-1 design, is where individuals receive interventions with the order or scheduling decided at random. This allows one to observe the impact an intervention has on individuals and between individuals over time, and allows theoretical interpretations to factors that cause these changes (Craig *et al.,* 2008).

Miguel and Kremer (2004) address how to deal with contamination or spillover effects of the intervention to those outside the intervention arm. They suggest that this should be addressed in the study design, and use the example of a public health intervention involving deworming school children. Previous reviews on deworming have concluded that there is little evidence to show deworming has a positive effect on school attendance. However, Miguel and Kremer found that deworming significantly decreased school absenteeism and is therefore a cost-effective way to improve school participation. Their explanation for this difference in outcome is that other studies had randomised the intervention at an individual level, so failing to account for potential benefits a child who had not been dewormed was gaining from his or her dewormed fellow students. If any benefits of the deworming programme extended to the children in the control arm then the effects of the intervention were not seen. In this case, children who were not in the programme benefited from dewormed students in the same school as their chances of acquiring worms decreased. They suggest that this pilferage/ spillover of benefits to those in the control arm can be corrected for by randomizing at a higher unit level, so for example randomizing at the school level instead to the individual level, therefore clustering at the school level. This would mean that all children in the same school would be in the same arm, therefore any externalities amongst pupils will be captured in each school. Changing the level at which one randomises may reduce spillover effects, however when clustering at a higher level, one should bear in mind that the level of spillovers that can be corrected for is limited and so cannot be used to control for spillovers that occur at a more global level (Miguel & Kremer, 2004).

Other obstacles mentioned above in carrying out an RCT can be addressed in similar practical ways. For example, to be able to improve their sensitivity in evaluating rare outcomes, sample sizes can be increased where possible; to address lack of generalisability, over restrictive patient eligibility criteria can be relaxed by undertaking more pragmatic trials; to encourage uptake, participants and providers can be encouraged to participate in studies by using more acceptable participation and enrolment terms; and political and legal obstacles can be addressed through persuasion. Suggestions on how to tackle a variety of RCT obstacle have been addressed in various literatures (Stephenson *et al.,* 1998; Black 1996; Bonell *et al.,* 2010).

3.5.2: Plausibility Design

Like RCTs, plausibility designs also use comparison groups to draw causal inferences, however in plausibility studies randomisation is not used to identify the treatment and control groups. Instead a treatment group may already have been identified and a control group will then be selected to match the treatment group either at the beginning or during the implementation period or afterwards at the analysis stage. The inclusion of a control group allows for inferences on incremental impacts of the programme to be analysed (CDC, 1999; Victoria *et al.,* 2004; Black, 1996).

One of the main shortcomings of plausibility studies is that their levels of internal validity may not match those of RCTs for various reasons. By not randomly assigning intervention and comparison groups, plausibility studies are less able to account for the influences of chance, confounding or bias to their outcomes (Eccles *et al.,* 2003; Habicht *et al.,* 1999). To be able to account for this, the intervention and comparison groups should be similar in all characteristics apart from exposure to the intervention, however due to lack of randomisation of individuals or groups into each arm it is difficult to ensure this (Rosen *et al.,* 2006). In plausibility studies, where an intervention group is matched to a comparison group, selection into the comparison or intervention arm may be driven by the participant or provider of the intervention. This is fine if reasons as to why individuals or groups are put in each arm are given, as this can be controlled for in the analysis. However, when selection leads to unobservable differences in characteristics between the control and intervention arm, differences cannot be controlled for, and the study outcomes may therefore not reflect the true outcomes of the intervention, as they may only be due to the differences between the two arms

(Rosen *et al.,* 2006; Ravallion, 2006). The same is true for plausibility studies that use the same people initially as a comparison and then as an intervention group. Changes may occur to the group over time, making their characteristics different between baseline and post-intervention.

Spillover effects are a possible limitation seen not only in RCTs but also in plausibility studies. Depending on the type of intervention, its effects may spread to those in the comparison group, dampening the true outcomes of the intervention. An example of this can be seen in Maharashtra, India where in 2005 the government rolled out an 'Employment Guarantee Scheme' (EGS). The scheme was designed to provide employment and a salary to anyone as long as they were willing to work. The wage rate for the scheme was considered low and therefore it was believed to be self-selecting to the income poor. However, the EGS ended up creating a lower bound wage distribution where on a national scale workers would not take up work offering salaries lower than that provided by the scheme. Without consideration of this spillover effect, an evaluation of this scheme would reveal that the EGS had no impact since the difference in wages had not changed between participants and non-participants. However, this interpretation underestimates the effects. The true outcome was that the scheme did increase the wages of the poorest in society, but it also lifted the lower wage rate for those in the control arm who were more income rich. When relatively comparing wages, the gap between the income poor to the rich did not change but when comparing baseline wages in the poor to post-intervention wages, an increase in wages was observed (Ravallion, 2006).

Another problem may arise if the placement of the intervention is determined by a proxy means test. A proxy test may be used to determine who qualifies as a possible study participant to receive the intervention, and is a function of observed characteristics. It can be assumed that all those who have a similar proxy test have similar characteristics. If uptake for all those who have the required proxy test is 100% then there will be no individuals left to be placed in the control group who have similar characteristics to those in the intervention, leaving comparisons to take place between individuals who do not share the same proxy test score (Ravallion, 2006).

It is argued that, to answer the question of whether an intervention has an effect under ideal circumstances (i.e. to look at the efficacy of the intervention), the best study to use would be an RCT where the intervention will be implemented in carefully selected and restricted areas and under close supervision. Plausibility studies are thought to be better at measuring the effectiveness of a study, in other words, whether the intervention will have an effect under real life situations (Bryce *et al.,* 2004). The overall result of such a plausibility study will look at how the context in which the intervention is implemented affects its outcome (Barreto *et al.,* 2005; Black, 1996).

The advantages and limitations mentioned above refer to plausibility studies in general. There are various sub-sets of plausibility study designs, each with its additional advantages and disadvantages. The three most common designs used are: uncontrolled before and after studies, controlled before and after studies and time series designs (Eccles *et al.,* 2002; Habicht *et al.,* 1999).

Uncontrolled before and after studies: With this design a survey is carried out before and after the introduction of an intervention in the same study site(s). Any differences observed between the two surveys are equated to the effect of the intervention (Eccles *et al.,* 2003). Although this study is named 'uncontrolled', this may be a bit mis-leading as the same study site acts as the historical control arm (before implementation of the intervention), and the intervention arm (after implementation of the intervention). This type of study is considered relatively simple to conduct and superior to observational studies, which will be explained further on. Their main limitation is that secular trends or changes within the study group may not be detected making it hard to attribute observed change to the intervention (Eccles *et al.,* 2003; Rosen *et al.,* 2006, Victoria 2010).

Time series design: This design can be used when a comparison group cannot be identified, for example after the dissemination of national guidelines or mass media campaigns. Intervention groups are selected and followed up with data collected at several time points before and after the intervention. The data collected after implementation of the intervention will allow for the effects of the intervention to be assessed, by controlling for any underlying cyclical trends that have been identified through the pre-intervention data collection activities (Eccles *et al.,* 2003; Cousens *et al.,* 2011). The accuracy of this design improves with increasing number of data entry points, therefore it is useful where routine data sources are available. There are situations where data collected close in time are more similar to those collected far apart. This is known as auto-correlation and can create biases in interpretation of the data. To reduce this bias, data collected between time points prior to the intervention should be collected over a sufficient amount of time. In addition autocorrelation effects can be allowed for in time series regression models and auto regressive integrated moving average (ARIMA) modelling. What time series designs cannot do is control for changes occurring after implementation of the intervention (Eccles *et al.,* 2003).

Controlled before and after studies: As with RCTs, a control population is identified containing similar characteristics to the intervention population, however the selection is not done randomly. Data are collected from both populations before and after implementation of the intervention, and observed differences seen in the data are assumed to be due to the intervention. This design is also known as the double difference or difference in difference estimator, where the difference between the mean differences from each arm is seen as a result of the intervention (Ravallion, 2006). Limitations to this design include that because the decision of where to implement the intervention may not be in the hands of the evaluators, it may not be evident who will form the intervention and the comparison group in the survey. One solution is to have an informed guess when designing the sampling for the baseline (Eccles *et al.,* 2003). Another solution is to carry out a 'within group' analysis where baseline and post-intervention data are compared within and not across each group. Results from such an analysis should be interpreted with caution because if the comparison and control groups are not similar then they may not experience the same secular changes, therefore any conclusions made about the intervention's effect may in fact be false (Eccles *et al.,* 2003). The double difference estimator method can also be used to identify biases in randomised controlled studies. It can be used to confirm that there are no selection or compliance differences or biases between the control and intervention arms (Ravallion, 2006).

Case control studies: This study uses retrospective data and would be best used in situations where an intervention has already been implemented. In such studies, a group experiencing the intervention's outcome (cases) are compared to a control group without the same experiences (control). Retrospective data are then used to assess those exposed to the intervention in the case and control group and this is then used to calculate the likelihood of experiencing the outcome if exposed to the intervention (Bonell *et al.,* 2011).

3.5.2.1: Plausibility Studies: Improving Programme Designs

Certain analyses techniques have been developed which can be used to improve the usefulness of plausibility studies. This section will mention a few of these techniques.

The Propensity score matching method (PSM) is a way of ensuring that the comparison group chosen to match the intervention group are of similar characteristics, increasing the probability that any differences seen between the two are purely as a result of the intervention's effects. To briefly describe this method, participants' characteristics are chosen based on economic, social, political and other factors that may influence the assignment of the programme. These may be run through a logit or probit regression to determine each participant's propensity score (PS). Participants in the intervention group are then matched to a comparator with a similar PS. Outside of plausibility studies, PSM can be used in RCTs to provide insight into how random the selection process for the intervention has been, by comparing the PS of those in the intervention and control arms (Ravallion, 2006; Bonell *et al.,* 2011; Cousens *et al.,* 2011).

Discontinuity designs can be used in controlled before and after studies. They are useful with interventions that need to be assigned to participants with certain characteristics, for example extra tuition for school children who get test scores below a certain level or anti-poverty programs targeted at those who earn below a certain income level. In discontinuity designs, pre and post evaluation data are collected for the intervention group which has been defined by certain characteristics, and a comparison group that forms those who fall outside of the required characteristics, but are close to the relevant thresholds. Changes seen between pre and post evaluation data are compared between the comparison and intervention groups. The effect of the intervention is measured by how much the difference in the outcome in the intervention group varies from the difference observed in the comparison group (Ravallion, 2006).

Pipeline comparisons is a method that can be used when the implementers are unable to supply the intervention to all those who would like it and qualify to receive it, for example due to resource constraints. It can also be used where the intervention is being introduced in a staggered way, where all those who successfully applied for the programme may not receive it at the same time. The selection process in this design means that all those who qualify have very similar characteristics. Those that have already received the intervention can then be compared to those who are yet to receive it. An assumption made with this design is that the timing of treatment allocation is random. To ensure that the comparison and intervention groups are similar one can carry out the propensity score analysis. Pipeline comparisons may also be combined with discontinuity designs where the intervention's cut off points for selection change in a progressive manner as development takes place, therefore as the cut off points modify, the current intervention group is compared to the current comparison group (Ravallion, 2006).

The Instrumental Variable (IV) technique is used to better estimate causal effects in observational studies when analyses carried out directly between treatment and outcome may be biased by reverse causality, unobserved variables or measurement error. An IV is a variable that is logically related to, and statistically correlated with the treatment variable, but does not necessarily have to be directly linked to the outcome. The ideal IV will be void of biases present in the treatment variable. An example of use of an IV would be in the study carried out by Leigh et al where the effect of smoking status on health in a population was estimated indirectly through the use of cigarette price as an IV (Ravallion, 2006; Leigh *et al.,* 2004; Cousens *et al.,* 2011).

3.5.3: Adequacy Design

Adequacy studies are also known as observational studies. In this design, there is no assignment of participants into intervention or comparison groups. Instead the intervention is implemented on a population and what is key to these designs is that the outcomes evaluated from the study population are compared to previously established adequacy criteria to see if they have been met. An example of criteria include absolute outcomes such as: the intervention should distribute 10 million packs of oral rehydration therapy to children with diarrhoea; or may refer to change, for example the intervention should result in a 20% point decline in reported diarrhoea deaths. Adequacy studies can either be cross sectional, where data are collected at a single time point, or longitudinal where more than one measurement is taken over a given period of time to detect any trends (Habicht *et al.,* 1999). The design is useful in situations where more complex designs are not required, when the evaluators have a very limited budget, not much time to carry out a more detailed investigation or where human resources and skills available will not be able to support a more complex analysis design. The outcomes from adequacy studies allow for decisions to be made on whether more analyses need to be done using more complex methods to further identify reasons for the intervention's effects, or reasons for failure to meet expected criteria (Habicht *et al.,* 1999).

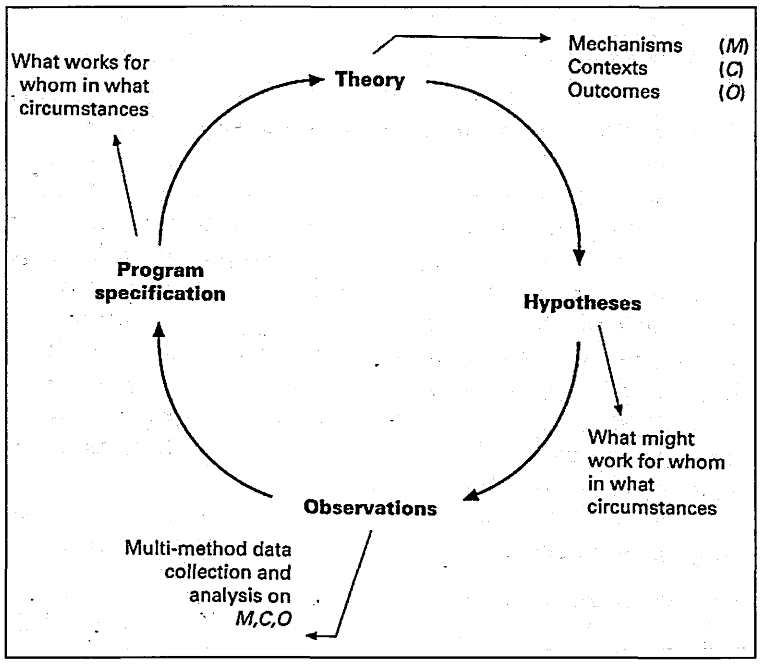
The advantages of these types of studies are that no resources need to be used in finding a good comparison group; the nature of the design is such that an evaluation can take place just with secondary data, meaning in some instances that no data collection activities need take place; and due to a low requirement for resources these studies tend to be cheaper and less time consuming. However, these advantages come at a cost. Because this design does not control at all for bias, chance or confounding, it does not allow for an interpretation of association to be made between the intervention and outcomes seen. The interpretation of the outcome results in this type of study is limited to giving information on whether the expected changes have taken place or not. Further explanations as to how or why certain outcomes were seen have to be sought through more complex designs. Since adequacy studies do not have a comparison group, it may be difficult to conclude that the outcomes seen are purely as a result of the intervention or due to other contributing factors experienced during the implementation of the intervention, such as general socio-economic improvements or secular trends in the study population such as mortality or malnutrition. Not having a comparison group means that the study may not always reveal positive outcomes of the intervention. For example, if an intervention is implemented under deteriorating socio-economic conditions, the outcome of the evaluation may reveal that the intervention has not had an effect when in fact the lack in change may be due to the programme being effective in providing a safety net for the affected population (Habicht *et al.,* 1999).

Victora *et al.,* (2011) suggest methods of data collection in programme evaluation, designed for the developing world that is suitable for plausibility and adequacy studies and can be used in settings where control areas are not possible because all areas are scaling up the same programmes and many programmes may be scaling up at the same time. Their proposed methods use the district as the unit of design since the district is usually considered as the main administrative unit of health programmes in many countries. The process involves continuous monitoring of the programme with evaluations taking place at an interim and summative period. Data will be collected from the district level through the use of existing national databases that may need to be developed further. National level data will be obtained from government headquarters such as the ministry of health, while more local data can be obtained at the provincial level. These data can be compared for accuracy. Cost data can be obtained directly from the programme implementers. Additional data collection methods such as household surveys and health facility assessments may be necessary to allow specific indicators to be measured and assess data quality from the existing data. The broad range of data collection activities will allow for data to be analysed in a variety of ways including health outcome estimates, dose-response relationships and modelling. Contextual factors can also be incorporated. Victora *et al.,* (2010) feel that the incorporation of government into the various processes of the evaluation will support country ownership of the programme and encourage human and structural development. The evaluation also builds on existing data collection activities which makes the process cost effective; the continuity of data collection and evaluation allows the programme to be moulded to fit the changing environment, making it sustainably effective; and the method of data collection creates independence for the evaluators, easing control from programme funders (Victora *et al.,* 2011).

3.5.4: Other Study designs

In understanding process, all study designs should incorporate a process evaluation which should be carried out to high methodological standards with outcome reported comprehensively. A process evaluation may play a significant role in unravelling study findings. Such an evaluation may help identify factors that could have contributed to unexpected study findings or help in understanding important external factors that make an intervention a success or failure, and the mechanisms of these factors in influencing the study outcomes (Craig *et al.,* 2008). An example of type of process evaluation is explained by Pawson and Tilley (1997). They suggest a method of evaluation known as 'realistic evaluation', which is designed to better predict patterns of outcomes of a programme given the context it is implemented in and the mechanisms used to implement it. The evaluation claims to do this by trying to answer deeper questions at each step of the evaluation cycle. Currently, a typical traditional evaluation cycle will start by framing a theory, from which a hypothesis is postulated. This hypothesis is then tested through observations of various kinds, and the observations are then used to make empirical generalizations. The generalizations may or may not conform to the expected form of theory; if not then the theory will have to be re-framed. The realistic evaluation cycle has similar steps, however each step includes more content. For example, the theory step looks further into the underlying mechanism of how the programme may function, the context in which the programme should be implemented to be effective, and how these factors may affect outcome; the hypothesis stage looks at 'what might work, for whom, and in what circumstances'; the observations carried out will consist of many methods and types of analyses to obtain data on the programme outcomes, in relation to the observed mechanism of the programme and context. The observations will then be able to determine what works for whom, and under what circumstances, in relation to that specific programme (Pawson & Tilley, 1997).

Figure 3.1: The realistic evaluation cycle (courtesy of Pawson & Tilley (1997)



Another form of evaluation suggested by Deaton, 2009 is that experiments be used to estimate parameters, and these parameter should be incorporated into theoretical models to determine the outcomes of the programmes under certain conditions (Deaton, 2009). An example of the use of this technique is by Duflo, Hanna and Ryan (2008) who used their experimental findings on improving teacher attendance in India to construct a model to aid in understanding teacher behaviour. This model has been used by others to interpret their experimental findings (Todd *et al.,* 2006).

3.6: CONCLUSION

There is no internationally agreed formula on deciding which study design to implement when evaluating public health interventions. Evaluation of public health interventions is not always straight forward as they tend to come with a range of relevant research questions which cannot be answered by just one study design. An added complexity is that understanding the context in which the outcomes were created is also of great importance (Black, 1996; Mills *et al.,* 2008; Victora *et al.,* 2004).

What can be deduced from the above is that the decision on which design to use is based on a variety of factors. These include the questions that need to be answered (some designs answer certain questions better than others), and the level of confidence required in answering the questions: RCTs tend to give a higher level of confidence in interpretation of the outcome compared to the other less controlled studies. The feasibility of carrying out a study is also an important consideration. Feasibility ranges from the resources made available for the evaluation, how the implementers have decided to roll out the intervention, the ethics of the design and the willingness of the politicians and community to provide the necessary support (Black, 1996; Victora *et al.,* 2004; Moore *et al.,* 2011; Sanson –Fisher *et al.,* 2007).

It has been suggested that if possible, public health researchers should draw on the strengths of all studies and use a mosaic of the different designs to come up with conclusions of the intervention. Plausibility studies can be used then to show an association between the intervention and outcomes observed in the adequacy study. More expensive RCTs can be used at the end to test for a causal hypothesis (Habicht *et al.,* 1999; Rychetnik *et al.,* 2002; Vandenbroucke, 2008).

Regardless of the method/ design used to evaluate an intervention, the quality of the study is of great importance (Rychetnik *et al.,* 2002). The same weight placed on deciding which design is best to evaluate an intervention should also be given to how rigorously the study design is implemented. An example of where the choice of design was considered appropriate but the outcome of the evaluation was misleading because of poor quality of evaluation is in health financing. A few plausibility studies were highly regarded as providing evidence that user fees in health had potential benefits, and these studies were used in promoting policy reforms that supported user fees. However, more careful analyses of the data revealed the presence of confounding and inappropriate economic specifications. It became clear that the data provided poor evidence to support the use of user fees in other contexts, not because of the choice of design but because the poor quality of study implementation (Mills *et al.,* 2008). The importance of having high quality studies, regardless of the design used has been addressed by guidelines such as the CONSORT, TREND and STROBE which provide information on how to improve the rigor of pragmatic RCT, quasi experimental and observational studies (Zwarenstein *et al.,* 2008; Rosen *et al.,* 2006; Mills *et al.,* 2008).

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CHAPTER 4

STUDY SITE AND METHODOLOGY OVERVIEW

This chapter includes a description of the study design, the intervention that was implemented and timelines for each aspect of the study. Also included are explanations of the techniques used to select the study areas, collect and analyse the data.

4.1: STUDY SITE

The study was conducted in three districts in Western province in Kenya: Busia, Butere-Mumias and Teso[1] (Figure 4.1). These areas were selected because of their high malaria endemicity; the presence of relatively active retail markets; the absence of other malaria treatment interventions; and the familiarity of the implementation team with the local areas. Within Western province, Bungoma district was excluded because of the extent of previous malaria-related interventions which may make it atypical. Mount Elgon district was excluded because of the then political insecurity in that area.

Table 4.1: Study district demographics

	BUSIA	TESO	BUTERE/ MUMIAS
NO. OF SUB-LOCATIONS	99	83	79
% OF SUB-LOCATIONS RURAL	76	66	75
% HOUSEHOLD HEADS COMPLETED PRIMARY SCHOOL	57	54	58
NO. OF HEALTH CARE FACILITES*	39	21	51
% POOR (RANGE ACROSS SUB-LOCATIONS)	67 (53-74)	50 (44-68)	62 (53-73)
ESTIMATED POPULATION 2007 (AVERAGE PER SUB-LOCATION)	370,608 (4,964)	227,058 (2,769)	573,275 (7,350)
POPULATION DENSITY/ KM^2	433	406	611

* These include Ministry of Health and other ministries, mission and non-governmental health facilities (CBS, 1999; Noor *et al.*, unpublished data)

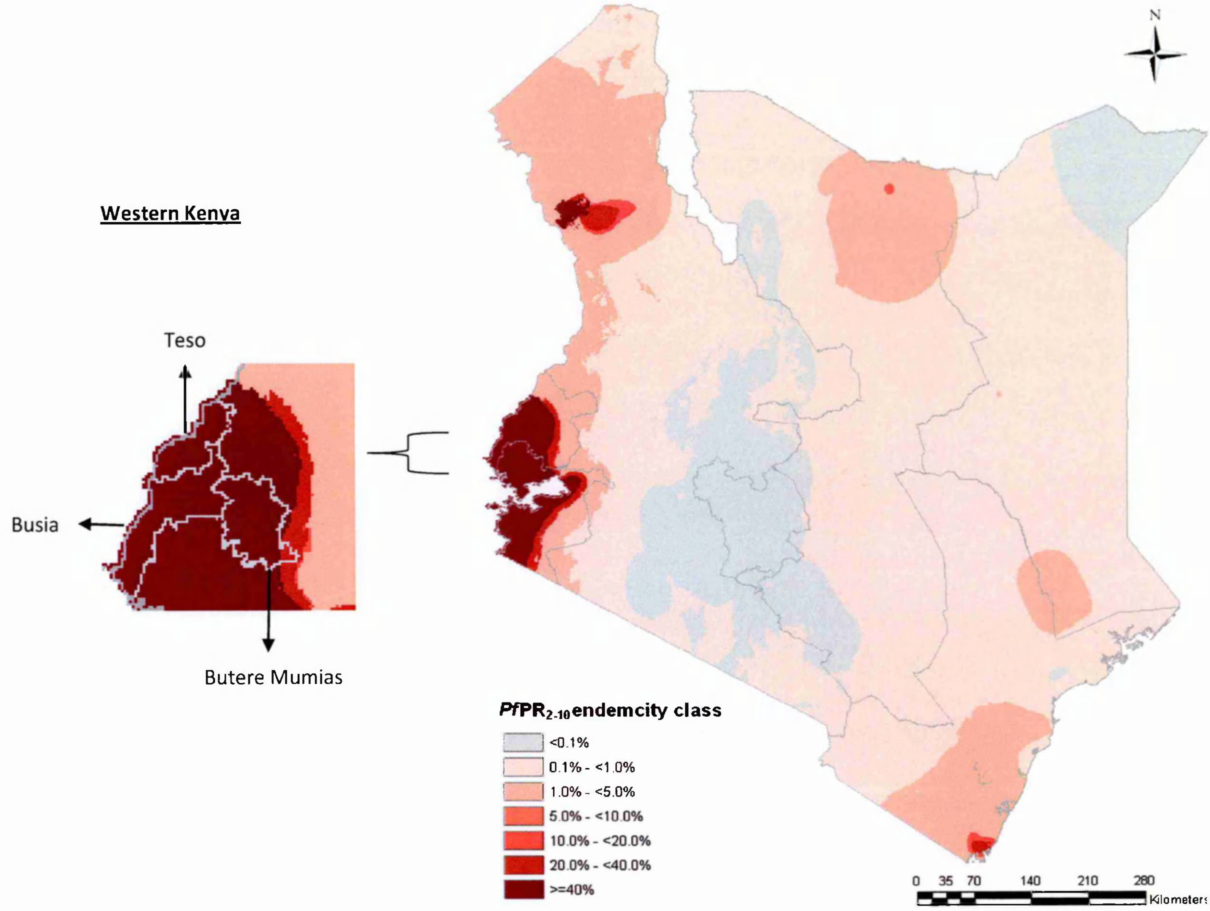
The percentage of the population living below the poverty line in the study districts averaged 67% in Busia, 62% in Butere-Mumias and 50% in Teso, with population densities per km^2 of

[1] each of these districts has been officially divided into two or more districts since the intervention began

433, 611 and 406 respectively (Table 4.1). The western region of Kenya suffers from the highest malaria prevalence in Kenya, with *Plasmodium falciparum* parasitaemia prevalence in children aged 2 to 10 years greater than or equal to 40% (Figure 4.1). At the time of the survey, Butere-Mumias had 51 government health facilities, Busia 39 and Teso 21, consisting of dispensaries, health centres and one district hospital per district (Noor *et al.,* unpublished data). In 2009, across the 3 districts, school attendance averaged 45% (country's average 40%), the percentage with access to piped water averaged 6% (country's average 30%), the percentage who owned a mobile phone was 51% (country's average 63%), the percentage owning a radio was 71% (country's average 74%) and an average of 54% claimed to have some sort of employment (country's average 52%). Not much difference was observed between the districts.

As with other areas of Kenya, all government health facilities in the study sites were supposed to supply AL for free to patients, although stock-outs and unofficial fees were common (Kangwana *et al.,* 2009, Chuma *et al.,* 2009). Malaria diagnosis was predominantly clinical in both public and private health sectors (Zurovac *et al.,* 2008; Wasunna *et al.,* 2008).

Figure 4.1: Map of Kenya showing the district boundaries for Western Kenya and parasitaemia levels across the country



Courtesy of Noor *et al,* (2009) predicted parasite rate (PR) among 2-10 year olds based on a geo-statistical risk model.

4.2: STUDY DESIGN

The intervention was implemented at the sub-location level. The study employed a pre-post cluster randomised controlled design, with randomisation occurring at the sub-location level, which is the fifth and lowest administrative level in Kenya, governed by a sub-chief. A randomised controlled trial was used because the randomisation process ensures that all characteristics within the control and intervention arms are similar, minimising influences of chance confounding and bias seen in other studies. This significantly increases the reliability of the results. The strengths and weaknesses of using a cluster randomised controlled design in evaluating this intervention are discussed in more detail in Chapter 8. Randomisation occurred in clusters because the nature of the intervention is such that it could not be targeted at individuals. Therefore randomisation occurred in blocks consisting of groups of individuals, with some groups falling into the intervention arm and others into the control arm (see Chapter 3). Carrying out the study at this level allowed for a reasonable scale for implementation, contained the total medicine cost for the intervention and limited contamination between control and intervention areas, which would more likely occur if larger areas such as locations or divisions were used. The sub-locations included in the study had to be rural, since contamination would be better controlled in such areas, as opposed to supplying the drug in urban and peri-urban areas which represented between a quarter and a third of all sub-locations, and serve a wider population, including those who travel from surrounding sublocations to purchase medications. The populations within the sub-locations had to be between 2,500 to 10,000 (Table 4.2); smaller sub-locations were excluded to ensure there was a reasonable scale for implementation and adequate sample sizes for the evaluation; larger sub-locations were excluded to contain costs.

A modified randomisation process was used to select the study sublocations. A random list of all eligible sublocations was formulated per district in Microsoft Excel. The first intervention sub-location was selected from the top of the list. In order to reduce the potential for contamination a 'buffer zone' was created where all sublocations located within two sub-location boundaries of the selected sub-location were removed from the list. The list was reshuffled randomly and the first sub-location on the new list allocated to the control arm. The same procedure of creating a buffer zone around this sub-location was continued, alternating between the selection of intervention and control sublocations, until three intervention and three control sublocations had been selected within the district (Figure 4.2). The estimated population in the control and intervention arms were 38,620 and 44,538 respectively (average population per selected sub-location of 4,620, range 2,703 to 9,294) (*appendix 1*).

Table 4.2: Demographics for the selected sub-locations

SUB_LOCATION	DISTRICT	%POOR	UNIQUE_ID[1]	EST POP 2007	POP_DENSITY/ KM^2	ARM
Magombe central	Busia	64	89	3575	200	Control
Kanjala	Busia	68	36	2703	389	Control
Nanderema	Busia	66	74	3490	298	Control
Muyafwa	Busia	65	34	4053	473	Intervention
Lupida	Busia	68	2	4418	328	Intervention
Sikinga	Busia	69	10	5945	392	Intervention
Akachachata	Teso	48	23	2626	293	Control
Apokor(angurai)	Teso	51	2	3185	374	Control
Kamunuoit	Teso	49	61	3273	297	Control
Aludeka	Teso	48	48	3275	285	Intervention
Okatekok	Teso	52	75	3955	375	Intervention
Kakalet	Teso	49	18	3370	372	Intervention
Shianda(bm)	Bm	58	61	3030	748	Control
Buchifi	Bm	61	27	8659	574	Control
Musamba	Bm	62	3	8079	476	Control
Eshibinga	Bm	69	71	4134	643	Intervention
Lunza	Bm	61	31	9294	482	Intervention
Malaha(bm)	Bm	63	18	6094	612	Intervention

[1]Represents the numbers assigned to the sub-locations on the district maps below; BM=Butere Mumias

Figure 4.2: Maps of (a) Busia district, (b) Teso District, and (c) Butere-Mumias District, showing control (orange) and intervention (green) sub-locations. (N.B: 'Other' (see Legend) refers to all sub-locations that do not fit the sub-location criteria (e.g. urban or peri-urban and with populations <2,500 or > 10,000))

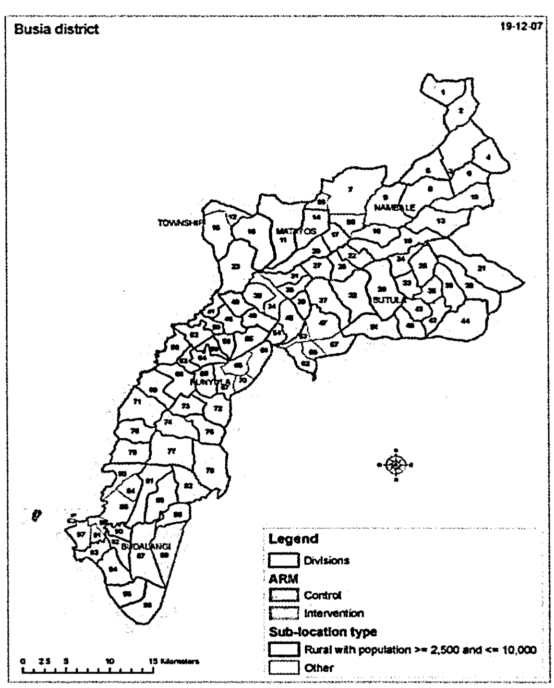


Figure 4.2a

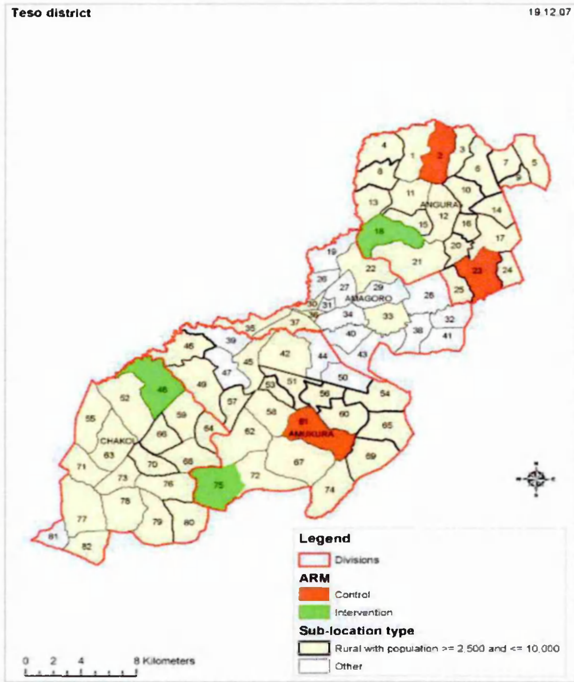


Figure 4.2b

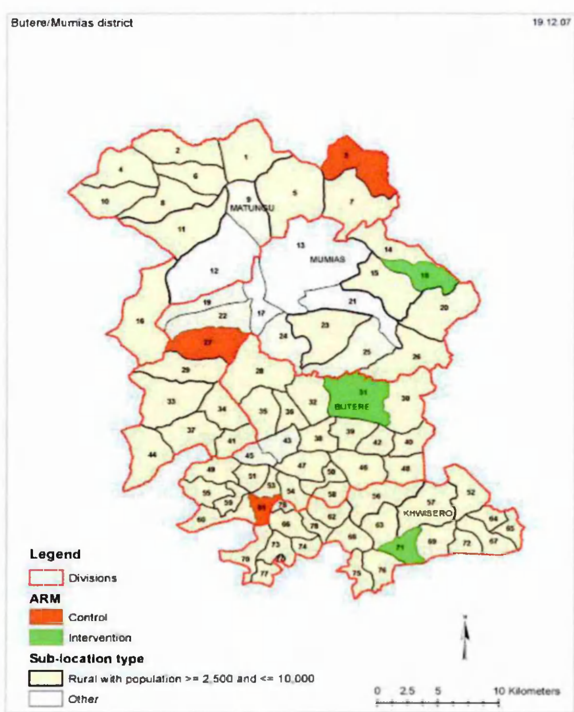


Figure 4.2c

The characteristics of the study sub-locations that were selected are displayed in Table 4.2. The populations within the selected Teso sub-locations tended to be less poor than the other two districts, with the percentage living below the poverty line ranging from 48-52%. In Busia the percentage living under the poverty line ranged from 64-69% while in Butere-Mumias it was from 58 to 69%. In Kenya, the poverty line (the cost of a basic basket of food and non-food items) in 2003 was about 1,239 KSH (15.25USD) per person per month for rural inhabitants (CBS, 2003). Butere-Mumias was the most densely populated with sub-location population densities ranging from 476 to 748 per KM^2. Busia and Teso's population densities were quite similar with Teso ranging from 293-374 per KM^2 and Busia from 200 to 473 per KM^2. Across the three districts, the average percentage poor and population densities between the control and intervention sub-locations were similar (Table 4.3).

Table 4.3: Comparison of percentage poor and population density between intervention and control sub-locations, across all three districts (CBS, 1999)

ARM	AVERAGE %POOR	AVERAGE POP_ DENSITY/ KM2
Control sub-locations	58	4291
Intervention sub-locations	60	4949

The intervention targeted retail outlets serving intervention sub-locations, which were identified through an outlet census carried out in May 2008. Outlets were included in the census if they were located in the intervention sub-locations or were just outside these sub-locations but were identified by key informants as serving their populations. Initial lists of retail outlets were sourced from the local public health officers, and updated with input from local chiefs and sub-chiefs. The lists were further amended after walking around the study areas with the village elders to confirm the presence of outlets and add missed outlets. The snowball technique was then used where each shop visited was asked about the presence of other outlets in their area. Finally, members of the community passing by were opportunistically asked about the location of outlets known to them. Enumerated outlets were invited for training if they had been functioning for a minimum period of six months, and reported selling antimalarials and/or antipyretics within the 12 months prior to the census. In the study areas these were found to consist of registered and unregistered pharmacies (referred to here as specialised drug stores), and general stores which sold medicines alongside general household goods. Similar outlets identified in the non-intervention sub-locations remained as controls. A second census was conducted in May 2009, to update the list of functioning outlets for the follow-up provider survey.

4.3: THE INTERVENTION

The intervention package was designed and implemented by the DOMC in collaboration with PSI, Ministry of Health (MOH) staff at the province and district level and other key stakeholders. The role of KEMRI Wellcome Trust Research Programme (KWTRP) was limited to evaluation. The three main components of the intervention were provision of subsidized packs of paediatric AL to retail outlets, training of retail outlet staff, and community awareness activities. No interventions were implemented in the control arm. In both intervention and control arms the policy of provision of free AL at government facilities continued unchanged.

4.3.1: The Product – Pre-packaged AL for children 3-59 months

PSI and the DOMC developed a branded pre-packaged AL product for the treatment of malaria in children. In line with dosing recommendations, two doses were developed: a yellow six tablet pack for 3 months to less than 3 year olds (5-15kg) and a blue 12 tablet pack for 3 to 4 year olds (15-25kg) (Figure 4.3a & b). The lower age limit of three months was set because at the time of the study, AL was not recommended in children under 5kg. Although the blue pack would be appropriate for children up to 7 years of age, the target group for this intervention was children under five years of age, being the most vulnerable age category to suffer from malaria. Additional consumer friendly information was added to the product's outer packaging using pictorials and instructions on safe use of the medication, in a form that was suitable for those with low literacy levels. The information was designed to promote appropriate dose recognition by caregivers and shopkeepers and promote adherence to the full regimen. The process of product development was based on extensive formative research and pre-testing, and modified in consultation with the case management team of the DOMC. The product's instructions also included details on the IMCI danger signs and the need to refer to the public health service severe conditions and children under three months. The AL was branded as Tibamal®, a pretested name derived from the Kiswahili words '*Tiba ya Malaria*', meaning *malaria cure.* Kiswahili is one of the official languages of Kenya which is commonly understood by all tribal groups in the country, including those participating in the study.

Figure 4.3: Additional consumer friendly information added to standard AL packaging for (a) blue 12 tablet pack (3-<5years of age); and (b) yellow 6 tablet pack (3months to <3 years)

Figure 4.3a

Figure 4.3b

4.3.2: Drug Regulation

At the time of the survey, AL was classified as a POM and could only be sold from registered pharmacies on furnishing of a prescription. However, despite this regulation it was not uncommon to be able to obtain the treatment without a prescription. For the purposes of this study, special dispensation was requested and granted from the Expert Committee of Clinical Trials within the PPB to allow for the treatment to be deregulated to an OTC treatment so that providers would be legally able to dispense the treatment without the requirement of a prescription.

4.3.3: Price

PSI sales staff delivered the treatment directly to selected outlets on a monthly basis at a subsidised wholesale cost of 8 Kenya Shillings (KSH) (0.10 US USD)[2] per treatment pack, both packs being the same price. The outlets were instructed to sell the packs at a retail price of 20 KSH (0.25 USD), and this price was printed on the drug packaging (Figure 4.3a & b). The retail price was set to provide outlets with a mark-up of 12 KSH (0.15 USD) per pack, equating to a 150% retailer mark-up, and was designed to be competitive with other available, but less effective monotherapies such as SP and amodiaquine, which were sold at around 30 KSH (0.37 USD) per full dose. The average retail price of AL without the subsidy was around 500 KSH (6.16 USD).

4.3.4: Distribution and Training

As described above, outlets were identified from the baseline retail census and selected for inclusion into the intervention if they had been functioning for a minimum period of six months and sold either an anti-malarial or antipyretic within the past year. A total of 225 outlets were selected in the intervention area, of which 61 were specialised drug stores

[2] Source of exchange rate: http://www.exchangerate.com/past_rates_entry.html.accessed 13/4/2010. On 1st Novermber 2008, when the subsidised drugs were first distributed, 1 US dollar was equivalent to 81.23KSH.

(registered or unregistered pharmacies) and 164 general stores (which sold medicine alongside general household goods). Outlet staff attended a one day malaria-related training offered between August to October 2008 covering clinical diagnosis, treatment, adverse drug reactions (ADRs) and patient referral. Training materials were developed by the implementation team, building on those used previously for shopkeeper training in Kenya (Marsh *et al.,* 2004). In addition, shopkeepers were supplied with two job aids, one an algorithm explaining steps to take if a child presented at the outlet with a history of fever, the other showing dosing schedules for both the Tibamal® packs. These job aids were designed to improve the quality and quantity of information given by providers to consumers. Retail owners were given the option to supply Tibamal®. From November 2008, subsidised AL was provided to trained retail outlets in packs of six tablets (for children aged 3-35 months) and 12 tablets (for children aged 36 to 59 months). Supportive supervision of the retailers by PSI took place in February 2009. This involved PSI trainers going to trained outlets and testing staff on information learnt during the training sessions. The purpose of this exercise was to assess retention of knowledge and to remind shopkeepers of key messages.

4.3.5: Supporting interventions

A series of promotional activities in the intervention areas and related dominant market centres was carried out by PSI. Messages targeted caregivers of children under five and promoted appropriate treatment seeking behaviour including the benefits of AL and its availability both in public sector facilities and identified private sector outlets. Messages were delivered through small group sessions and community leader workshops. The main community awareness activities began in March 2009, and then intermittently in August and September 2009. Activities were continued to the end of the pilot in May 2010. They consisted of nine community leader workshops that targeted 47 people; nine community events that targeted 11,500 people, ten small group discussions that targeted 200 people and outreaches carried out by community based organisations that targeted 21,000. These activities were designed to make the community aware of malaria, the availability of Tibamal®, and the importance of adherence to the medication. Tibamal® was also advertised through posters and paintings on shops that sold the treatment. Tibamal® branded headscarves, t-shirts and pens were also freely distributed to the intervention community (Figure 4.4) (*appendix 2*). Above the line communication strategies, which use media that are broadcast and published to mass audiences such as newspapers, television and radio were not used in this pilot to avoid possible contamination between intervention and control arms. In 2006/7 the government had carried out AL awareness campaigns across the country, so both arms had previously received some general information on the current malaria treatment policy (personal communication, Andrew Nyandigisi, DOMC, Ministry of Public Health and Sanitation Kenya).

Figure 4.4: Ladies from one of the intervention sub-locations wearing Tibamal® promotional items, standing in front of a Tibamal® wall painting

4.3.6: Pharmacovigilance

The PPB had developed guidelines and tools for the collection of pharmacovigilance data on AL since its release in the public sector. The intervention package was implemented in collaboration with the PPB to ensure that pharmacovigilance requirements were met.

Shopkeepers were supplied with a Daily Activity Register to document AL dispensed. Shopkeepers were also educated on possible adverse effects and were instructed to advise caregivers to seek care from the nearest health facility for any suspected ADRs. They were provided with CHW referral forms which were to be filled in and given to patients being referred to health facilities for suspected ADR symptoms, or failed AL treatment. A copy of the form was to remain at the outlet to be collected by the PSI sales staff and handed over to the PPB. All ADRs seen within health facilities were to be reported back to the PPB. The PPB along with district investigation teams were to be involved in following up any serious ADRs.

4.4: DATA COLLECTION

4.4.1: Field workers

Field workers were identified through job adverts circulated within the study districts, as well as using the snowballing technique, where potential field workers were asked whether they knew others who were willing and able to do the job. They were shortlisted for an interview based on their secondary school grades (Kenyan Certificate of Secondary Education (KCSE) B+ and above), their level of field work experience, and their ability to speak the required local dialect. Those either with a university degree or currently in university, meeting all the other requirements were more likely to be shortlisted. In total 20 field workers were selected per district. Selected field workers were trained on the purpose of the study, basic data collection techniques, and how to administer the informed consent forms and data collection tools. Training was supported by training manuals, role plays and mock interviews. Field workers worked in two teams of ten, with one person per group being assigned the role of a field supervisor. Field workers selected at baseline were retained to carry out follow-up surveys if their work at baseline was satisfactory. A second interview process was carried out at follow-up to replace field workers who had left after the baseline survey.

4.4.2: Survey indicators

Prior to this study, a list of key indicators for all operational research looking to improve access to anti-malarial treatment was developed in collaboration with the DOMC, and was approved by them (*appendix 3*). The indicators were divided into compulsory and optional indicators. The indicators were identified through consideration of relevant DOMC targets; GF indicators; RBM monitoring and evaluation reference group indicators; and Global ACT subsidy monitoring and evaluation frameworks. The compulsory indicators (*see appendix 3*) were to be monitored by all studies evaluating interventions to increase anti-malarial access outside the public sector within Kenya. The purpose was to standardise outcome measures between studies to allow for data to be compared, and to also ensure that the DOMC are provided with the relevant information required to inform policy. This study was designed to address all the compulsory indicators (*see appendix 3*) and some optional indicators that were considered to be relevant in monitoring the effect of the intervention. In this study, data collection activities used to provide outcomes for indicators consisted of household, mystery shopper and provider surveys. A context analysis was also carried out to comprehend the environment in which the intervention was being implemented and identify potential effect modifiers. FGDs took place at follow-up with caregivers and retailers to explore reasons for the impact observed and identify any challenges in the implementation process. This activity was not included as part of the thesis, however important findings from the discussions were used as part of the documentation of context, to better understand the effect of the intervention. The different surveys allowed for the intervention to be evaluated from the angle of the consumer, and through reported and observed behaviour of the provider. Data from the three surveys were then triangulated for a more comprehensive understanding of the intervention effect.

All surveys were conducted in July-August 2008 and July- August 2009 (Figure 4.5). In each district, the mystery shopper was conducted first, followed by the household survey and then the provider survey. Data collection for all the activities took place on questionnaires derived from similar studies, and amended to capture the desired information. Questionnaires for the household and provider surveys were translated into local dialects of the study communities (Samia for Busia district, Wanga for Butere-Mumias and Kiteso for Teso) and back translated to confirm the accuracy of the translations. The mystery shopper survey took place in the form of a roll play and the questionnaire completed afterwards by the fieldworker. The mystery shopper questionnaire was only in English. All tools were piloted in two sub-locations in Busia that had not been selected for the study, but resembled the study sub-locations, and changes made where necessary. The tools were piloted in April 2008 and April 2009. More details on the pilot are described in section 4.4.3.

Figure 4.5: Intervention and study timelines

Activity	June-July 08	Aug-Sept 08	Oct 08	Nov 08	Dec 08	Jan 09	Feb 09	Mar 09	Apr 09	May 09	Jun 09	Jul 09 – April 2010
Development and pretesting of training materials	X											
Training of private sector retailers		X	X									
Distribution of drugs				X	X	X	X	X	X	X	X	X
Community activities								X	X	X	X	X
Supportive supervision							X					

Baseline surveys: July-August 2008

Follow-up surveys: July-August 2009

Household survey: The household survey primarily addressed specific objectives 1 (To determine the impact on the proportion of children under five with fever being treated promptly with appropriate anti-malarial treatment, and adhering to the correct dose), and 3 (To determine distribution of benefits of retail sector delivery of AL by socio-economic status).

The primary indicator for this activity was defined as: 'the proportion of children aged 3 to 59 months reporting fever in the past two weeks who started treatment with AL on the same day or following day of fever onset'. Household surveys are increasingly using the "same day or following day" terminology to increase the feasibility of data collection as it is very difficult to collect data on the specific number of hours since symptom onset, as required by the original 24 hour formulation of the RBM indicator.

The household survey consisted of a structured questionnaire divided into seven sections. Section one captured characteristics of all members residing in the household. Residential members were defined as those who plan to live or who have lived in the household for a period of six months or more. Characteristics collected included identification of the household head, members' age and sex; mosquito net usage in the night prior to the interview; identification of the parents or guardians of members under 16 years; and identification of members that had suffered from fever within the last two weeks of the interview. The purpose of this section was to identify those who needed to be interviewed in the other sections of the questionnaire.

Section two collected further details on mosquito net use in the household. This included details on the net's source, net cost, and which nets had been treated with insecticide.

Section three captured information on household geography and demographics, and section four on assets owned by the household, to determine household wealth. Wealth assets included housing quality, sources of income, education status and ownership of livestock and amenities in the household.

Section five captured information on treatment actions caregivers took to treat their under five year old child's fever. Fevers were captured only if they occurred within the two week period prior to the interview, and had started within this period. The survey was restricted to fevers occurring in this period since the recall period beyond this time point is questionable (McCombie, 2002). Both resolved and unresolved fevers were captured. Details on the type of treatment sourced to treat identified fevers were documented. Types of treatments included: any action taken to try to relieve the child's symptoms, such as conventional treatment received from a doctor, nurse or any other healthcare professional; self-medication at home; treatments with home remedies; prayers or seeing a traditional healer. Other information collected in this section included any costs incurred for accessing treatment, whether advice was given from providers regarding any medication dispensed, and adherence practices of caregivers to any antimalarial received. Adherence was defined as giving the child the quantity of medicine as specified in the MOH treatment guidelines (DOMC, 2007). Both under and over dosing were considered as non-adherence. The timing of administration between doses was not considered as recall of specific times may have proved difficult, therefore increasing the potential for recall bias.

Section six assessed caregiver's knowledge on malaria treatment and diagnosis for children under five. It also identified where knowledge on malaria was gained from. Section seven captured information on the proportion of non-target household members receiving intervention AL.

The questionnaire was administered to different members of the household. Sections one to four were administered to the household head. The household head was identified as the person in the household who is acknowledged as such by members of the household and who is usually responsible for the upkeep and maintenance of the household. Sections five and six were administered to all caregivers within the household who had a child under five that had suffered a fever within two weeks prior to the interview. Section seven was administered to all members of the household who had suffered a fever within two weeks prior to the interview. In this section, where a child with a fever was below 16 years, information was collected from their parent or guardian. Written consent was obtained from all household heads or their representative, and verbal consent from all others who were interviewed. The village elders were informed about the survey in advance and aided the field team in identifying households to be interviewed.

Visual aids, consisting of pictures of common anti-malarial and anti-pyretic medication, nets, malaria related posters, calendars and leaflets were used to help field workers and the respondents to correctly identify malaria treatments and information education and communication material mentioned in the interviews. Birth charts were used to quickly calculate ages and calendars to determine dates of when fevers began and treatment sought.

Provider survey: The provider survey mainly addressed specific objective 2 of the thesis (To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five.)

The purpose of this survey was to assess the knowledge and practices of the provider when it came to the treatment of malaria. The provider survey consisted of a structured questionnaire divided into six sections. Section one captured details on the geographical location of the outlets. Directions to the outlet obtained from the retail census were included in this section to aid field workers in locating the outlet. Details captured in this section were compared to those in the retail census to ensure the right shop was interviewed. Section two captured information on the type of malaria related IEC materials available in and around the outlet. This included whether the outlet possessed any of the intervention's promotional materials such as posters, job aids and wall paintings. This section gave an indication of what information providers and caregivers using that outlet may be exposed to. Section three captured information of staff characteristics such as their age, level of education and health qualifications. The information gave an idea of the level of expertise available in the outlet as this may affect the quality of care received. Section four asked questions on the stocking of antimalarials in the outlet. The questions were designed to determine the median price charged for AL treatment, the proportion of outlets with expired AL in stock and the proportion of outlets reporting stock outs within the past 2 weeks. To assess the proportion of outlets with expired AL, all expiry dates of available AL, entered by batch number, were recorded. Stock outs were only recorded within the past two weeks to reduce recall bias. Stock outs were assessed by asking providers how many days over the past two weeks have they not had AL available. Only outlets that currently had AL stocks were asked this question. This section was also designed to assess if AL was being stored appropriately (appropriate storage refers to keeping medicines off the floor, in a dry area, away from direct sunlight, and with the packaging intact). Section five captured information on factors that determined which medicines outlets stock and sell to customers and how customers with insufficient funds were dealt with. The last section captured information on provider knowledge of malaria. This included knowledge of malaria diagnosis and treatment in children under five and adverse effects of AL. The questionnaire was administered to the shopkeeper present at the outlet at the time of the visit. If two or more providers were available in the outlet, the interview was administered to the one responsible for selling medication to customer. Written consent was obtained from the interviewee prior to interviewing.

Mystery shopper survey: The mystery shopper survey also addressed thesis objective 2 (To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years.)

The purpose of this study was to analyse the patient provider interaction to give better information on actual rather than self-reported provider behaviour. In this survey field workers, disguised as local residents visited selected outlets seeking treatment for a four year old child with fever. The fieldworkers presented the following scenario: *a 4 year old child (weighing 15kg), under their care who has been suffering from a recurring fever for 3 days, especially at night. The child had no other symptoms, and no medication had been given to the child so far.* The field worker was then to wait for the provider to ask further questions and/ or prescribe a medication. If no medicine was recommended, field workers were to prompt the provider to recommend a medicine. If after prompting no medicine was recommended then the field worker was instructed to find out reasons as to why. If a medicine was recommended then the field worker was to find out why the provider suggested that particular medicine. Details of the interview were discretely filled in on structured questionnaires away from the outlet, once the interview was completed. Questions asked on the questionnaire included whether the provider asked about any signs and symptoms of the disease to determine need for referral; what advice if any was given on how to treat the child's fever; details of each medicine sold including cost, quantity and the reason for it being dispensed; if AL was dispensed, whether information was given on how to administer it. The information allowed for an assessment to be made on the proportion of providers offering appropriate medication in response to malaria symptoms and providing appropriate OTC advice for this treatment.

This mystery shopper method was chosen instead of direct observation or exit interviews because it minimises any potential bias that may occur through knowing one is being observed. In addition, achieving a reasonable sample size for exit interviews could be very time consuming in outlets which receive very few fever customers per day. The mystery shopper technique did raise some ethical concerns as informed consent could not be obtained from the medicine seller at the time of the interview (Marsh *et al.,* 2004; Madden *et al.,* 1997;

Chalker *et al.,* 2000). Written consent was therefore sought from all shopkeepers during the retail census for their willingness in principle to participate in the mystery shopper survey. Outlets were informed on what the survey involved, however neither whether their shop was to be selected for the survey nor the date of the visit was revealed as this could have affected the study outcomes.

Documentation of context: Documentation of activities at national and district level which may have influenced the study outcomes in both the intervention and control areas was carried out in the form of a context analysis. Throughout the study, a series of desk-work analyses of newspaper articles, minutes to meetings, draft proposals, budget allocations and memos, as well as in-depth discussions with the DHMTs at the local level took place. From this, a chronology of events was documented, as well as a summary of the events, the locations and the duration. These data were taken into consideration during evaluation of the study outcomes.

4.4.3: Feasibility Study and Pilot

A three day feasibility study was carried out in December 2007 to counter check some of the assumptions made in the research proposal. The feasibility study was carried out to bring some clarity on the average number of retail outlets serving a rural sub-location, the percentage of these outlets selling antimalarials and antipyretics, the type of antimalarials available and the distance people will walk to seek antimalarial treatment. The information collected from this study was used to amend the proposal, where applicable.

A more comprehensive two week pilot study was carried out four months later, in April 2008, to test the tools' acceptability, and see if they were collecting the desired data; to get a clearer idea of the time lines, budget and workforce that would be required for the baseline survey; and to test the data entry screens. The pilot was carried out in Busia, one of the three selected districts for the intervention. Two sub-locations not included in the main study were chosen for the pilot. These study areas were separated by a distance of two sub-locations and displayed contrasting types of rural activity. The two were Alungoli, a sub-location with the 5th lowest rural estimated population (estimated for 2007) of 2,889 and Bukhalalire, with the 2nd largest rural population of 9,272. The percentage living in poverty in Alungoli was estimated at 67.3% while in Bukhalalire 64.8%. The distance between the two sub-locations was chosen to enable us to determine whether a buffer zone of 2 sub-locations was enough to limit contamination. In each of the two sub-locations, the following data collection activities were administered: the retail census, the household census (mapping), the household survey, the provider survey and the mystery shopper survey. The tools that were tested comprised all informed consent forms, all data collection questionnaires, the training manual and visual aid. A retail census was carried out to identify outlets selling medication and serving the study sub-location population. From the census, 20 shops were randomly selected where provider and mystery shopper surveys were carried out. One enumeration area (EA) was randomly selected in each sub-location. GPS mapping was done on every household in each of these EAs and the name of each household head was listed. From this list, random selections of 71 households were chosen per EA. Household survey questionnaires were administered to these selected households.

For each survey that was piloted, issues that were brought up during the pilot were addressed. The tools were also sent to PSI to confirm if they collected the type of data that would best answer the questions they were interested in. A similar pilot was carried out a year later, prior to the follow-up survey to test new questions added into the questionnaire.

4.5: DATA MANAGEMENT

Baseline data were captured on paper questionnaires and double entered into Microsoft Access (2007). Follow-up data only for the household survey was captured using personal digital assistants and Pendragon Forms version 5.1 (Pendragon Software Corporation, Libertyville, Illinois [http://www.pendragon-software.com] and downloaded onto Microsoft Access [2007]).

The questionnaire on the PDAs was designed to limit error through incorporating restrictions into what could be entered for certain questions, and notifications for missed questions. Both baseline and follow-up questionnaires were checked at the end of each day to maintain a high quality of work. Errors in the questionnaires that were identified as straight forward were corrected by the responsible field worker; more complicated errors resulted in the household or provider being re-interviewed. At the end of each survey, three to four days were allocated as 'call back' days. This time allowed for re-interviews where errors needed to be corrected, and it also allowed for households to be interviewed if members were previously absent.

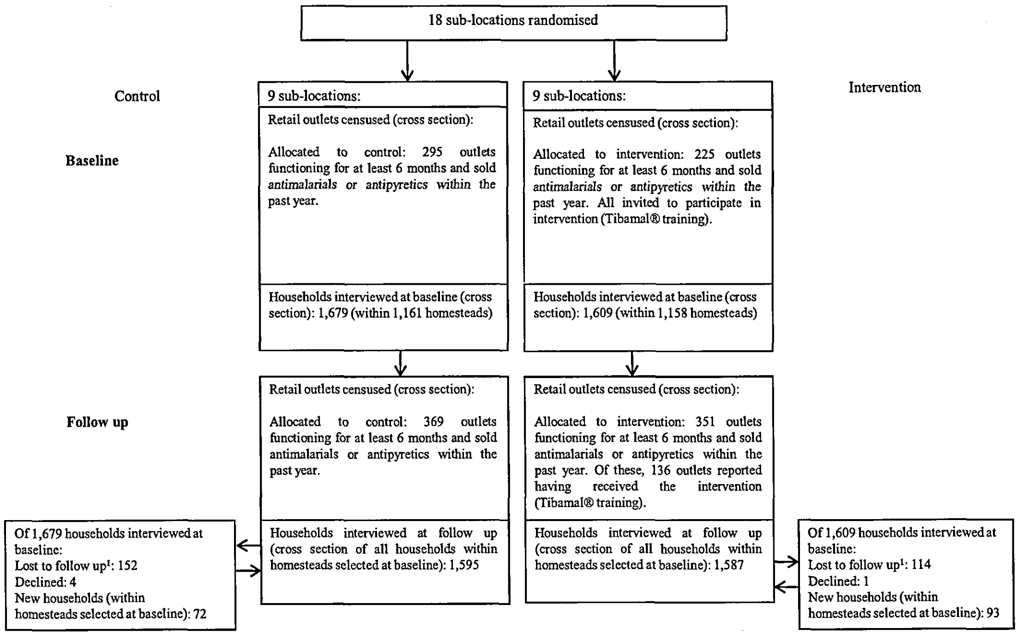
4.6: SAMPLE SELECTION

4.6.1: Sample selection: Household survey

The primary outcome was defined as the proportion of children aged 3–59 months reporting fever in the past 2 weeks who started treatment with AL on the same day or following day of fever onset. Secondary outcomes included the adequacy of AL doses obtained and consumed, and the price paid per pack. These were assessed using pre- and post-household surveys conducted in July–August 2008 and July–August 2009. The study was based on an intention-to-treat analysis where clusters were not adjusted or further selected depending on the proportion of retail outlets which actually received the intervention. The sample size was based on detecting a 20% point difference in the primary outcome, with 5% significance, 80% power, and an estimated design effect of 2 to account for the cluster survey design (percentage point refers to the absolute difference observed between two percentages, in this case between the outcome percentages observed between the intervention and control arm). I estimated that the primary outcome would be 20% at baseline (based on data collected by Gitonga *et al.,* (2007), and allowing for some increase since that survey took place). A design effect of 2 was considered conservative based on an intra-class correlation coefficient of 0.16 from a similar previous survey in Kenya (Gikonyo, KEMRI Wellcome Trust Research Programme, unpublished data), and an estimated 43 homesteads per cluster. This led to a required sample size of 158 childhood fevers in each arm, which I estimated would require data collection from 1,138 homesteads in each arm, equivalent to around 210 households per sub-location. A homestead is a group of households within the same compound belonging to a single extended family. A household consists of a person or a group of related or unrelated persons who live together in the same dwelling unit, who acknowledge one male or female as the head of the household, who share the same housekeeping arrangements, and who are considered to constitute one unit. A homestead can contain one or more households.

Three EAs were randomly selected within each intervention and control sub-location on the basis of probability proportional to population size. A homestead census was carried out in the selected EAs in May 2008 and each homestead was mapped using GPS hand-held receivers (Garmin etrex and Trimble 12 band GPS units). From the homesteads enumerated, 43 were randomly selected using simple randomisation with Excel 2007, within each EA. To achieve the sample size, homesteads selected for sampling but not available during data collection were replaced by the next available from a randomly ordered list of homesteads, formulated during the census. A pretested questionnaire was administered to all household heads within the selected homesteads to ascertain household socioeconomic status, and to all caregivers of children under 5 years of age reporting fever episodes in the 2 weeks prior to the interview to assess treatment-seeking behaviour and medicine use. All homesteads agreeing to participate at baseline were revisited at follow-up. All households within each homestead were interviewed at each time point, including new households that were established at follow-up (Figure 4.6).

Figure 4.6: Flow diagram showing households and retail outlets sampled and interviewed



[1]Households lost to follow up included those that had migrated out of the study area or were temporarily absent for the duration of the study.

4.6.2: Sample selection: Provider and Mystery shopper survey

The sampling frame for the provider and mystery shopper surveys was based on the retail censuses carried out in May 2008 and 2009 described above, when details of any anti-malarial medicines stocked, date of establishment and physical location of each outlet were recorded. Outlets were included in the sampling frame if they had been functioning for a minimum period of six months and sold either an anti-malarial or antipyretic within the past year, and all outlets in the sampling frame were included in the surveys. From the feasibility study, it was estimated that around 150 outlets would be surveyed in each group (i.e. control and intervention groups) (Figure 4.6).

4.7: DATA ANALYSIS

The data were analysed in STATA version 11 (College Station, Texas) by a two-stage process, with baseline and post-intervention data analysed separately. In the first stage a summary cluster measure was obtained for each cluster. The second stage involved comparing the sets of cluster-specific measures in control and intervention arms at follow-up using the unpaired *t*-test (Hayes & Moulton, 2009). A crude analysis was carried out on the cluster summaries using the simple two tailed t-test to obtain the means, 95% confidence intervals (CIs) and standard deviations (SDs) for the outcome of interest. In addition, an adjusted analysis was carried out at follow-up on all indicators using an individual level logistic regression run on the pooled data set (control and intervention arms). To control for potential confounders for each survey type, the following covariates were considered:

1) Provider survey: distance, outlet type (specialized drug store or general store) distance of shop to nearest road)

2) Mystery shopper survey: outlet type (specialized drug store or general store) distance of shop to nearest road), clinically related training and district

3) Household survey: patient age and sex, caretaker's and household head's education level, wealth score, bed net use last night, district, and, when adjusting for the adequacy of AL doses obtained and consumed, the source of treatment.

All covariates significant at a p-value of >0.2 were retained in the regression model. Baseline values for the outcome in question were also included as covariates if a difference of 5% points or more was observed between the arms at baseline. Adjusting for baseline values by including them as covariates in the regression analysis was selected as a more reliable approach than adjusting the values by analysing the change in the endpoint of interest (difference in difference approach). According to Hayes & Moulton (2009), analysis of change can be subject to the phenomenon of 'regression to the mean' where low values at baseline are expected to increase at follow up and high values decrease. These changes are due to random variation in measured endpoints and not the intervention. To explore the implications of this decision, where large differences were observed at baseline, the analysis was re-run using a difference in difference approach. In the difference in difference approach, adjustments are not made for covariates, so this analysis was carried out unadjusted. The intervention status of the cluster was not included in the logistic regression model. Rather, the regression model provided the predicted outcome in the absence of the intervention effect. Mean predicted and observed outcomes were obtained per cluster and residuals were obtained by subtracting the predicted outcomes from those observed in each cluster. The *t*-test was used on these residuals to assess the intervention effect, adjusted for the covariates included in the logistic regression model. The *t*-test was used for both crude and adjusted analyses, as it has been shown to be highly robust even for small numbers of clusters. A separate analysis allowing for clustering within homesteads was also conducted but did not affect the statistical significance of the results. Both crude (unadjusted) and adjusted analyses were carried out on all primary and secondary indicators, which were then used to calculate p values. All sub-analyses were kept descriptive due to their low sample sizes, and also to limit the running of multiple hypothesis tests on underpowered outcomes and therefore control for false significant outcomes.

As part of the household survey, the presence of certain household assets, selected on the basis of those included in the 2003 Kenyan Demographic and Health survey (DHS) (CBS, 2004) was recorded to assess the wealth of the household. The assets included source of water, type of toilet, amenities (electricity, radio, fridge, TV, bicycle, motorbike, car or truck, phone and solar power); household and land ownership, floor type, roofing material, type of cooking fuel and waste management. The PCA analysis run included all items as those included in the

DHS survey, except for whether a household had domestic help or not, which was omitted in error (*appendix 4*).

A wealth index was constructed by assigning weights to each asset using principal components analysis (PCA), with weights based on the first principal component only (Filmer & Pritchett, 2001). Each household was then assigned to a specific wealth quintile, those falling into the first quintile being most poor and those in the fifth quintile being least poor. All interviewed households were included in the PCA, regardless of whether they contained children under five, but the PCA was conducted separately for baseline and follow-up surveys to allow for the wealth of new households present at follow-up to be calculated. There are a variety of alternative methods for measuring socio-economic status, such as evaluating consumer expenditure or income, participatory wealth ranking and self-assignment. The advantages and disadvantage of these techniques have been described in Howe *et al.,* (2012). The PCA methodology was selected because this technique provided a more stable long term view of wealth of a household, which will not be influenced as much by short term economic fluctuations that may affect other measurements such as income or expenditure. In addition, this technique provides a simple and reliable way of measuring wealth with minimal influence of bias as data are collected on observation rather than solely relying on response from the interviewee. Finally, this technique has been widely used in similar surveys, which allows for comparability of findings from this study to others.

In the analysis I tested for heterogeneity in the effect of the intervention across wealth quintiles using ANOVA on cluster percentages for the primary outcome.

Calculating distances

Distances of homesteads to the nearest retail outlet (specialised drug store or general store) stocking AL was calculated using data from the retail census which was carried out in May

2008 and May 2009, and the household census carried out in June 2008. Homesteads and retail outlets were mapped using handheld global positioning system (GPS) (Garmin etrex, Garmin Ltd., Kansas, USA). Three readings within an accuracy of below 10.0 meters were taken, and an average derived as the final reading. Current estimates indicate that the accuracy of GPS readings is within 15 meters of the true position (Noor *et al.,* 2005).

Ancillary spatial data on roads, rivers, digital elevation model (DEM) and land cover (e.g. forest, large water bodies, cultivated fields, cultivated trees and aquatic areas) were used in calculation of travel time from homestead to the nearest AL retail outlet. Road data within the study area were classified according to three surface conditions: tarmac (very good or good condition), gravel (fair condition), and natural or earth surface roads (poor or very poor condition). A DEM obtained from Shuttle Radar Topography Mission (SRTM) (http://srtm.csi.cgiar.org/) (Huggel *et al.*, 2008) at a 90 meter spatial resolution was used to derive elevation while different land use and land cover classes such as forests, grass land areas, shrubs and crop cover were derived from FAO Africover land cover map (available at http://www.africover.org/LCCS.htm (Fao, 2000)). These different GIS layers were first combined into a single land use or land cover layer and various travel speeds assigned to various classes representing different modes of transport such as walking or motorised transport.

Travel time grids were then calculated using Access Mod version 3 (Ray and Ebener, 2008). The model applied a correction for walking on earth surface roads, crop and grass land areas while a correction for motorised transport was applied to tarmac roads, an anisotropic model corrected for elevation for up slope and downslope movement (Tobler, 1993). The resulting travel time grid was used to calculate cumulative extract travel time (minutes) from homesteads to retail outlets using ArcGIS (ESRI, Redland, CA, USA) spatial analysis tools. Finally, travel times were converted into ground distances (kilometres) at a rate of 5 km/hr^{-1}. 5

km/hr rate has been used in previous studies (Noor *et al.*, 2003) and was recommended in national policy guidelines for monitoring access (Ministry of Health, 1997). These distances were then used in subsequent analyses.

Euclidean (straight line distances): Distances from retail outlets to nearest roads were calculated using the Euclidean tool in ArcGIS (ESRI, Redlands, CA, USA) spatial analysis tool. The resulting Euclidean grid was used in spatial analysis extraction tools to calculate distance of retail outlets to the nearest road.

4.8: ETHICAL APPROVAL

Ethical approval was obtained from the Kenya Medical Research Institute Ethical Review Committee (# 1361), the Kenya Pharmacy and Poisons Board Ethical Committee for Clinical Trials (# PPB/ECCT/08/07), and the London School of Hygiene and Tropical Medicine Ethical Review Committee (# 5288). The study is registered with the International Standards Randomised Controlled Trial Number (# ISRCTN59275137). Informed consent was obtained from all by respondents for each activity has been as described discussed in the above, under in section 4.4: data collection.

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CHAPTER 5

PROVIDER SURVEY

5.1: INTRODUCTION

This chapter reports the results of the provider survey of drug outlets. The purpose of these surveys was to assess the knowledge and practices of the provider when it came to the treatment of malaria, contributing to addressing the second specific objective of the thesis: To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years. Full details of the methods for the provider survey are presented in Chapter 4. To briefly recap, a provider survey questionnaire was administered to retail outlets identified from the retail census, two months after the retail census, at baseline and follow-up. The questionnaire was administered to the member of staff present at the outlet. If more than one member of staff was available then the main employee responsible for selling medications to clients was selected. Outlets were included into the provider survey sample if they had been functioning for a minimum period of six months prior to the start of the retail census and had been selling either antimalarials or antipyretics within the past year. Written consent was obtained from the interviewee at the start of the interview and village elders were informed about the survey in advance.

The results are presented in section 5.2. Section 5.2.1 describes the characteristics of the outlets interviewed. Sections 5.2.2 and 5.2.3 look at the effect of the intervention on the awareness of interviewees about AL and Tibamal®, as well as the availability of AL and antimalarial monotherapies. Section 5.2.4 looks at the interventions effects on AL drug management issues, such as storage and retail price. Section 5.2.5 to 5.2.8 look at how the intervention has affected provider knowledge of malaria including diagnosis, treatment and referral practices, knowledge of treatment of malaria with AL and how it should be dispensed, its possible ADRs, and the documentation of malaria cases. Section 5.2.9 looks at factors that determine what antimalarials providers stock and sell to customers, and what action they would take if a customer had insufficient funds to purchase appropriate antimalarial treatment. The results are discussed in Section 5.3.

5.2: RESULTS

5.2.1: Shop Characteristics

Table 5.1 shows the total number of outlets selling an antimalarial or antipyretic by sub-location, identified from the retail census at each study time point. Overall there were 196 more outlets identified at follow-up than baseline. At both time points Teso had the least number of outlets per sub-location, averaging a mean of 30 at baseline and 39 at follow-up. Butere-Mumias and Busia had a similar number of outlets. In Busia the mean number of outlets was 39 at baseline and 48 at follow-up while in Butere-Mumias it was 32 at baseline and 45 at follow-up.

At both time points and in both arms general stores constituted the most common type of retail outlet, forming 77% of all outlets at baseline and 80% at follow-up (Table 5.2). As previously described, only outlets that had reported having functioned for a minimum period of six months were included into the sample frame for the survey. At baseline this constituted a total of 295 and 225 in the control and intervention arms respectively, and at follow-up 369 and 351 in the control and intervention arms respectively (Table 5.3).

Of the outlets included in the sampling frame, a total of 468 were successfully interviewed during the provider survey at baseline, 263 in the control arm and 205 in the intervention arm.

Table 5.1: Total number of retail outlets identified in the selected sub-locations (from the retail censuses)

District	Sub-Location	Arm	Number of outlets selling antimalarials or antipyretics in the past year –Baseline	Number of outlets selling antimalarials or antipyretics in the past year- Follow-up
BUSIA	Kanjala	Control	52	58
	Nanderema	Control	49	58
	Magombe central	Control	33	43
	Muyafwa	Intervention	26	44
	Sikinga	Intervention	38	44
	Lupida	Intervention	34	63
BUTERE MUMIAS	Buchifi	Control	26	40
	Shianda	Control	53	52
	Musamba	Control	30	44
	Malaha	Intervention	25	38
	Lunza	Intervention	32	55
	Eshibinga	Intervention	24	43
TESO	Akachachat	Control	31	38
	Kamunuoit	Control	26	49
	Apokor	Control	33	39
	Aludeka	Intervention	27	35
	Okatekok	Intervention	36	38
	Kekalet	Intervention	25	37
		Total	600	818

Table 5.2: Total number of retail outlets selling antimalarials or antipyretics in the selected sub-locations, by type

	Baseline		Follow-up	
Number of outlets by type:	Control n	Intervention n	Control n	Intervention n
Specialised drug store	66	71	77	89
General store	267	195	343	308
Other[1]	0	1	1	0
Total	333	267	421	397

Other= a bicycle repair shop and an agrovet.

At follow-up 639 retail outlets were interviewed, 319 in the control arm and 320 in the intervention arm. General stores constituted more than 70% of all shops evaluated at baseline and follow-up, and specialised drug shops made up almost all the remainder (Table 5.4). These numbers form the denominators for the following figures and tables in this chapter.

The average mean distance of retail outlets interviewed to the nearest road (any road excluding footpaths) was 188 and 327 meters in the control and intervention arms respectively at baseline, and 203 and 231 respectively at follow-up (Table 5.5).

Table 5.3: Outlets successfully interviewed, by outlets selected for the study at baseline and follow-up (functioning for 6 months or more)

	Baseline		Follow-up	
Number of outlets by type:	Control n (%)	Intervention n (%)	Control n (%)	Intervention n (%)
Specialised drug store	49/53 (92.5)	53/59 (89.8)	56/69 (81.2)	74/79 (93.7)
General store	214/242 (88.4)	152/165 (92.1)	262/299 (87.6)	246/272 (90.4)
Other[1]	0	0/1 (0)	1/1 (100)	0
Total	263/295 (89.2)	205/225 (91.1)	319/369 (86.4)	320/351 (91.2)

[1]Other= a bicycle repair shop and an agrovet

Table 5.4: Distribution of outlets successfully interviewed, by type (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Baseline		Follow-up	
Percentage of outlets by type:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Control (N=9) % (SD)	Intervention (N=9) % (SD)
Specialised drug store	19.6 (8.4)	26.2 (16.3)	17.8 (7.3)	22.9 (8.7)
General store	80.4 (8.4)	73.8 (16.3)	81.9 (7.6)	77.1 (8.7)
Other[1]	0 (0)	0 (0)	0.3 (1.0)	0 (0)

[1]Other= a bicycle repair shop

Table 5.5: Distance of interviewed outlets from nearest road (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Baseline		Follow-up	
	Control (N=9) mean (SD)	Intervention (N=9) mean (SD)	Control (N=9) mean (SD)	Intervention (N=9) mean (SD)
Distance from outlet to the nearest road (meters)	187.7 (123.8)	326.6 (286.9)	201.6 (121.5)	231.4 (98.8)

The mean number of staff serving customers was just under 2 (Control: 1.9 (SD:0.2), 1.8 (SD:0.2): Intervention: 1.9 (SD:0.1), 1.9 (SD:1.9); baseline and follow-up respectively). Respondents were asked whether members of staff who often or occasionally serve customers had any kind of clinical related training (Table 5.6). Clinical related training was classified as those who had some kind of nurse, pharmacy or medical training. Nurse training included a range of qualifications from certificate courses to full degrees; pharmacy training included pharmacists and pharmacy technicians; and medical doctor training included clinical officers as well as fully qualified physicians. There were no significant differences between the arms in the percentage of outlets that had at least one member of staff with a particular type of training, and percentages did not alter greatly from baseline to follow-up. Having some kind of nurse related training was the most common type of training received, with a mean of 11% of outlets having staff with this type of training at baseline and 13% at follow-up. Most of the qualified staff were working in specialised drug shops (*appendix 5*). A mean of one quarter of outlets at baseline and follow-up, averaging across the arms, had at least one member of staff who was either uneducated or had not completed primary school, and less than 4% of outlets had a child below 16 years usually or occasionally serving customers (Table 5.6). Appendix 5 contains analysis of the important outcome indicators carried out below, by outlet type.

5.2.2: Tibamal® training and awareness

As part of the intervention, one or more staff from retail outlets selected to participate in the intervention attended a one day training course. In order to identify outlets that had been trained on Tibamal®, respondents were asked whether they or any of their colleagues had received any type of health related training, including training on Tibamal®. As expected therefore, at follow-up, there was a significantly greater percentage of outlets reporting to have a trained member in the intervention arm (43%; n=136) compared to 1% (n=3) in the control arm (Table 5.7). It should be noted that unless otherwise stated, results are presented below for all retail outlets surveyed in the intervention arm, as opposed to just those with staff who attended the Tibamal® training.

Table 5.6: Educational background and age of staff who usually or occasionally serve customers (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of outlets with at least one employee occasionally/ usually serving customers with:	Control (N=9) % (SD)	Intervention (N=9) % (SD)
Any clinical related training[1]:		
Baseline	21.3 (8.1)	23.5 (18.8)
Follow-up	15.7 (6.7)	18.9 (8.4)
Pharmacy/ pharmacy related training[2]:		
Baseline	10.3 (7.0)	10.9 (8.8)
Follow-up	7.2 (4.2)	5.5 (5.0)
Nurse/ Nurse related training[3]:		
Baseline	10.9 (7.5)	11.9 (11.4)
Follow-up	10.7 (7.3)	14.8 (7.0)
Medical doctor training[4]:		
Baseline	1.3 (2.3)	2.7 (2.1)
Follow-up	0.7 (2.1)	1.0 (1.5)
Primary school incomplete or no education:		
Baseline	26.3 (11.6)	28.8 (17.0)
Follow-up	23.5 (11.3)	28.5 (12.6)
Below 16 years of age:		
Baseline	3.5 (5.8)	3.3 (3,5)
Follow-up	3.4 (3.5)	2.1 (2.7)

[1] Any clinical related training consists of: pharmacy, nurse and medical doctor related training; [2] Pharmacy related training includes pharmacy studied to a certificate or diploma level; [3]Nurse related training includes studying nursing to a certificate level (nurse aid) and diploma level; [4] Medical doctor training includes clinical officer who studied medicine to a diploma level

Table 5.7: Percentage of outlets that had at least one Tibamal® trained staff (mean of cluster summaries from the 9 intervention and 9 control clusters)

Tibamal® training:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Baseline	-	-	
Follow-up	1.0 (2.0)	43.1 (10.8)	42.1 (34.4, 49.9)

Respondents were asked whether they had heard of 'AL' or 'Tibamal®'. Across the arms at baseline, an average of 71% had heard of AL, which increased to 77% at follow-up, with no significant difference observed between the arms (unadjusted p=0.8222; adjusted p=0.7122) (difference in means: 1.1%; 95%CI: -8.8, 10.9) (Table 5.8). After adjusting for outlet type, the p value remained insignificant. At follow-up, 14% of respondents had heard of Tibamal® in the control arm and 92% in the intervention arm, resulting in a significant difference in

Tibamal® awareness between the arms (p=0.0001) (difference in means: 77.6%; 95%CI: 67.7, 87.6).

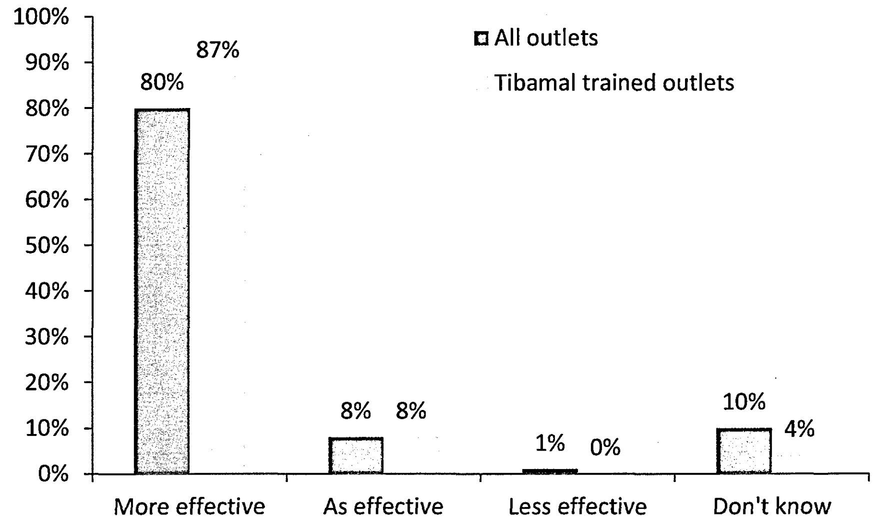
Table 5.8: Percentage of respondents that had heard of AL and Tibamal® (mean of cluster summaries from the 9 intervention and 9 control clusters)

Knowledge of AL and Tibamal®:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95%CI)	P-value Unadjusted *Adjusted*
Heard of AL:				
Baseline	74.1 (10.2) 119	68.5 (9.3) 140		
Follow-up	76.4 (9.0) 243	77.5 (10.7) 244	1.1 (-8.8, 10.9)	0.8222 *0.7122*
Heard of Tibamal®:				
Baseline	-	-		
Follow-up	13.9 (11.2) 44	91.6 (8.6) 289	77.6 (67.7, 87.6)	0.0001 *0.0001*

Of those who had heard of AL in the intervention arm, 80% of all outlets and 87% of just Tibamal® trained outlets thought it was more effective than other antimalarials (Figure 5.1). Of those who had heard of both AL and Tibamal® in the intervention arm at follow-up, 34% thought Tibamal® was more effective than other AL brands, with 40% stating that Tibamal® was equally effective compared to other AL brands (Figure 5.2). When Tibamal® was compared to other antimalarials, 81% of all outlets and 95% of Tibamal® trained outlets thought Tibamal® was more effective than other antimalarials (Figure 5.3).

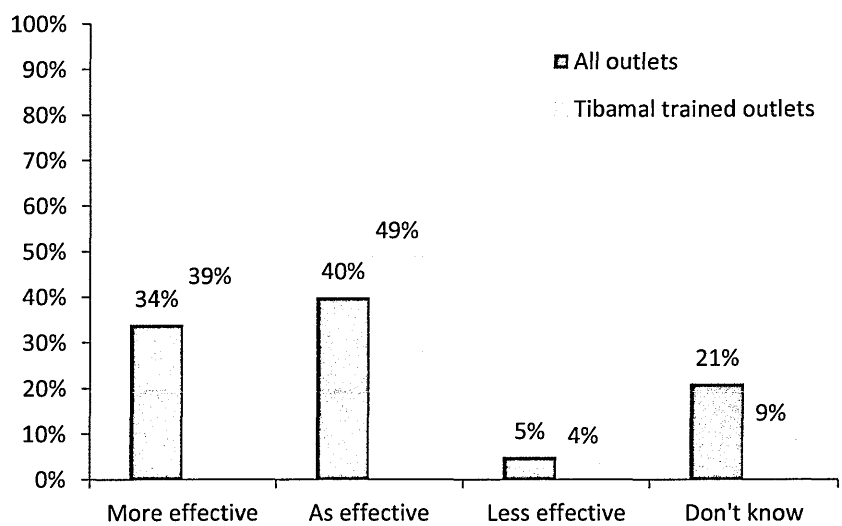
Tibamal® promotional items such as posters and job aids had been distributed to outlets and the Tibamal® logo and colours painted on or near some Tibamal® trained outlets. By the end of the intervention, PSI reported to have distributed 6,500 posters and calendars, 500 job aids, 51,000 square feet of Tibamal® wall branding/ paintings, and other items which included 5,418 headscarves, 3,938 T-shirts and 2,000 pens. At follow-up in the intervention arm, 37% of retail outlets were observed to be in possession of a Tibamal® poster or calendar, 22% possessed a Tibamal® job aid, and 8% possessed other items including Tibamal® t-shirts, head scarves or pens. A Tibamal® wall painting could be observed from the entrance of 45% of the shops. The majority of these promotional items were found at Tibamal® trained outlets (Figure 5.4), and no promotional items were found in the control arm.

Figure 5.1: Respondents' perception of the effectiveness of any brand of AL compared to other antimalarials in the intervention arm at follow-up (of those who had heard of AL*) (mean of cluster summaries from the 9 intervention clusters)



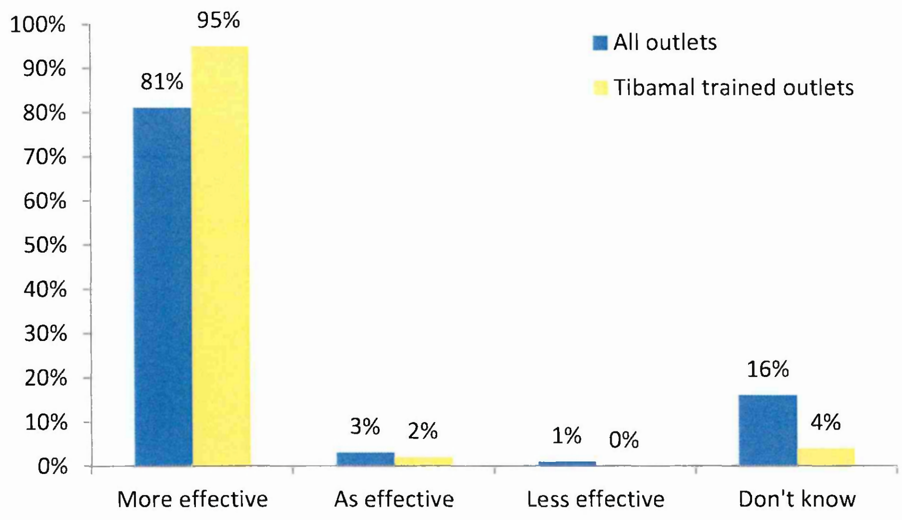
n=control=243; intervention=244

Figure 5.2: Respondents' perception of the effectiveness of Tibamal® compared to other AL brands in the intervention arm at follow-up (of those who had heard of AL and Tibamal®) (mean of cluster summaries from the 9 intervention clusters)



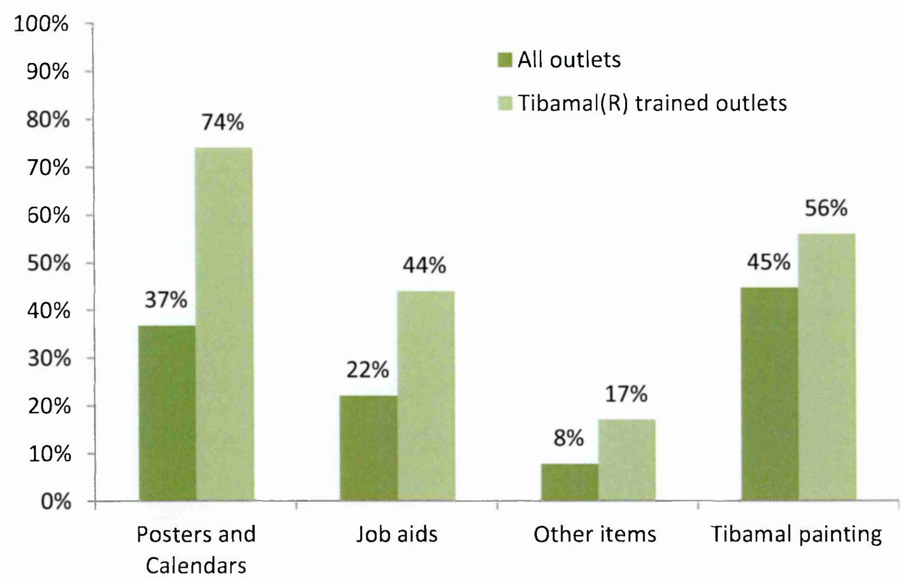
n=control=35; intervention=229

Figure 5.3: Respondents' perception of the effectiveness of Tibamal® compared to other antimalarials in the intervention arm at follow-up (of those who had heard of Tibamal®) (mean of cluster summaries from the 9 intervention clusters)



n=control=44; intervention=289

Figure 5.4: Tibamal® promotional items present in retail outlets in the intervention arm at follow-up (mean of cluster summaries from the 9 intervention clusters)



Other items include pens, head-scarves and t-shirts available in the outlet.

5.2.3: Antimalarial availability in retail outlets

I assessed whether there was a difference in the percentage of retail outlets with any type of antimalarials in stock at the time of the interview, between the arms. At baseline, the percentage of outlets with antimalarials in stock was relatively similar between the arms with 53% (SD:12.0) and 65% (SD:10.3) in the control and intervention arms, respectively. However, at follow-up there were significantly fewer outlets in the control arm with antimalarials in stock compared to the intervention arm p=0.0008 (difference in means: 16.3%; 95%CI: 24.6, 2.9) (Table 5.9).

Table 5.9: The percentage of outlets found with one or more antimalarials in stock (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of retail outlets with antimalarial in stock:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)	P value Unadjusted *Adjusted*
Baseline	52.8 (12.0)	64.6 (10.3)		
Follow-up	39.8 (10.23)	56.1 (6.0)	16.3 (7.9, 24.6)	0.0008 *0.0364*

[1]P value refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up

I then assessed which antimalarials were more likely to be found in stock. Of the monotherapies, amodiaquine was the most available at baseline, found in 50% (SD:10.6) and 58% (12.4) of outlets in the control and intervention arm, respectively. However, by follow-up, the availability of amodiaquine had dropped by more than half across both arms, making sulphadoxine-pyrimethamine the most commonly stocked monotherapy at 23% (SD:10.8) and 30% (SD:3.9) in the control and intervention arms respectively. Apart from amodiaquine, the availability of all other monotherapies remained relatively similar from baseline to follow-up and across the arms. Quinine was present in around 10% of outlets, CQ and the artemisinin monotherapies remained rare at less than 5%. As for the combination therapies, AL was stocked in less than 3% at baseline across the arms; by follow-up stocks had increased to 38% (SD: 12.4) in the intervention arm, but were significantly lower in the control arm at 6% (SD: 3.7) (p value: 0.0001). The increase in AL stocks observed in the intervention arm was predominantly due to Tibamal® stocks. The availability of other artemisinin combination therapies was less than 3% from baseline to follow-up and across both arms (Table 5.10).

Table 5.10: Availability of antimalarial monotherapies and combination therapies (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of retail outlets with specified antimalarials in stock:	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
Amodiaquine:			
Baseline	49.6 (10.6)	57.6 (12.4)	
Follow-up	18.7 (8.8)	14.2 (5.5)	-4.4 (-11.8, 2.9)
Sulphadoxine-pyrimethamine:			
Baseline	29.2 (8.7)	37.9 (10.5)	
Follow-up	23.2 (10.8)	29.5 (3.9)	6.3 (-1.8, 14.4)
Quinine:			
Baseline	10.8 (5.7)	11.2 (5.6)	
Follow-up	10.7 (4.9)	10.8 (5.5)	0.0 (-5.2, 0.5)
Chloroquine:			
Baseline	1.0 (2.1)	2.6 (7.7)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Artemisinin monotherapy:			
Baseline	4.7 (4.6)	2.8 (2.2)	
Follow-up	2.5 (15.7)	1.6 (12.4)	-0.9 (-3.1, 1.3)
AL (including Tibamal®):			
Baseline	0.5 (1.2)	2.4 (4.6)	
Follow-up	5.5 (3.7)	37.6 (12.4)	32.1 (23.0, 41.3)
Tibamal®:			
Baseline	-	-	
Follow-up	0 (0)	35.5 (11.9)	35.5 (27.1, 43.9)
Other ACT:			
Baseline	0.8 (1.6)	0 (0)	
Follow-up	2.1 (2.8)	0.4 (1.1)	-1.7 (-3.9, 0.4)
Other[1]:			
Baseline	0.5 (1.4)	0 (0)	
Follow-up	0 (0)	0.2 (0.7)	0.2 (-0.3, 0.7)

[1]Other= Proguanil

Unexpired AL (including Tibamal®) stocks at baseline were found in only 0.5% of outlets in the control arm and 1.5% in the intervention arm. By follow-up, AL stocks had increased to 37% in the intervention arm but to only 5% in the control arm. No stocks of Tibamal® were found in the control arm, but in the intervention arm, Tibamal® was present in 36% of outlets. The difference in availability of unexpired AL between the arms was significant at a p value of 0.0001 (difference in means: 32.1%; 95% CI: 23.0, 41.3). When adjusted for outlet type, the p values of availability of AL and unexpired AL remained unchanged at 0.0001. Less than 1% of outlets had expired stocks of AL in both arms and at both time points (Table 5.11). A test for interaction indicated that outlet type was not a potential effect modifier for the percentage of outlets with unexpired AL ($p>0.05$ at baseline and follow-up).

In the sub-sample of Tibamal® trained outlets, 72% were found to be stocking AL, 69% of which was Tibamal® branded AL (Table 5.11). 9% of all outlets in the intervention arm at follow-up were out of stock of Tibamal® at the time of the interview but reported usually stocking the drug (calculated as the difference between the percentage of retail outlets with unexpired stock (35.5%) and the percentage of outlets claiming to usually stock Tibamal (44.1%)) (Table 5.11). This was also true for one shop in the control arm. 21 outlets in the intervention arm and 1 in the control arm at follow-up did not report having any staff attending the Tibamal® training however, they mentioned that they usually sold Tibamal®, and of these, 15 in the intervention arm were found with stocks of unexpired Tibamal®. Stocks of Tibamal® were not available in 16% of the sub-sample of trained Tibamal® outlets who claimed to usually stock this medication (Table 5.11).

5.2.4: AL drug management

Outlets stocking AL were assessed to see if the treatment was being stored appropriately. The definition of appropriately was all AL packs kept off the floor, out of direct sunlight, in a dry area and with packaging intact. At follow-up, 79 and 82% of outlets were observed to be storing all AL stocks appropriately in the control and intervention arms respectively (Table 5.12). Expired AL stocks did not seem to be a problem, with less than 1% of outlets in both arms and timepoints having expired stocks of AL (Table 5.11). Storage conditions of AL in Tibamal® trained outlets were similar to those observed in all outlets in the intervention arm. Stock outs of AL within 2 weeks prior to the interview date were experienced in 33% of the 119 outlets stocking AL at follow-up in the intervention arm, with a median of 5 days of continuous stock out (Table 5.13). Only one (6%) of the 19 outlets stocking AL in the control arm at follow-up reported experiencing a stock out of AL which lasted for three days (Table 5.12).

The median cost of a tablet of AL at baseline was 14.58 KSH (0.18 USD) in the control arm; by follow-up this had fallen slightly by 3.54 KSH (0.04 USD) to 11.04 KSH (0.14 USD). In the intervention arm the cost of an AL tablet fell from 12.57 KSH (0.15 USD) at baseline to 3.33 KSH (0.04 USD) at follow-up, a difference of 9.24 KSH (0.11 USD) (Table 5.13).

Table 5.11: Availability of AL in retail outlets (mean of cluster summaries from the 9 intervention and 9 control clusters)

AL availability:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95%CI) n	P value[1] Unadjusted *Adjusted*
Percentage of retail outlets with AL (including Tibamal®) in stock:				
Baseline	0.5 (1.1) 2	2.4 (4.6) 5		
Follow-up	5.5 (3.7) 19	37.6 (12.4) 119	32.1 (23.0, 41.3)	0.0001 *0.0001*
Tibamal® trained outlets	-	72.1 (11.4) 99	-	-
Percentage of retail outlets with unexpired AL (including Tibamal®) in stock:				
Baseline	0.5 (1.1) 2	1.5 (3.2) 3		
Follow-up	5.2 (4.0) 18	36.8 (13.1) 117	31.7 (22.0, 41.3)	0.0001 *0.0001*
Tibamal® trained outlets	-	69.9 (12.4) 97	-	-
Percentage of retail outlets with unexpired Tibamal® in stock :				
Follow-up	0 (0) 0	35.5 (11.9) 111	35.5 (27.1, 43.9)	0.0001 *0.0001*
Tibamal® trained outlets	-	69.3 (11.9) 96	-	-
Percentage of outlets claiming to usually stock Tibamal® at follow-up[1]:				
Follow-up	0.3 (0.9) 1	44.1 (12.6) 139	43.8 (34.9, 52.7)	0.0001 *0.0001*
Tibamal® trained outlet	-	85.3 (12.6) 118	-	-

[1] This variable includes outlets that usually sell Tibamal® but may have been out of stock at the time of the interview.

Table 5.12: AL storage and stock outs at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

AL storage and stock outs:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)	P value Unadjusted *Adjusted*
Percentage of retail outlets storing all packs of AL appropriately:	78.8 (24.7)[1]	81.9 (17.0)	3.1 (-18.6, 24.9)	0.7626 *0.7357*
Tibamal® trained outlets	-	83.2 (16.6)	-	-
Percentage of retail outlets with AL available, reporting stock outs of any of the AL packs within the past 2 weeks:	6.3 (17.7)[1]	32.5 (18.1)	24.0 (3.6, 44.4)	0.0088 *0.0023*
Tibamal® trained outlets	-	32.5 (18.3)	-	-

[1]cluster summaries from 8 cluster; Denominators: control=19; intervention=119; Tibamal ® trained outlets=99

Table 5.13: Median stock out days and tablet price of AL at follow-up (cluster summaries from the 9 intervention and 9 control clusters)

	Control (N=9) Median (25%, 75% IQR)	Intervention (N=9) Median (25%, 75% IQR)
Median stock out days over the past two weeks in outlets where AL was available on the day of interview	3 (3, 3)[1]	4.9 (4.2, 8.1)
Retail price per AL tablet -KSH (including Tibamal®):		
Baseline	14.58 (4.17, 25.0)	12.6 (5.0, 20.13)
Follow-up	11.04 (7.29, 12.5)[1]	3.33 (2.5, 3.33)

[1]cluster summaries from 8 cluster; Denominators: control=19; intervention=119

5.2.5: Provider Knowledge of Malaria cause, symptoms and prevention

Respondents were asked to list all factors they thought caused malaria and factors that would prevent malaria (Table 5.14). Correct responses were based on what was taught during the Tibamal® training sessions. At baseline 6% in the control arm and 11% in the intervention arm were able to correctly mention malaria being caused only by a parasite in mosquitoes. These percentages remained relatively similar at follow-up, with no significant difference observed between the arms. A larger number of respondents (averaging 65% in both arms and time points) stated that malaria was caused by mosquitoes. More than 90% of respondents in both arms at baseline mentioned sleeping under a net as one way of preventing malaria, and this percentage remained similar at follow-up. The use of insecticide residual spraying and mosquito repellent were mentioned by less than 20% of respondents at both time points and across both arms. There was no significant difference in knowledge of preventive measures across the arms, nor was there a difference in knowledge in the sub-sample of outlets that attended the Tibamal® training in the intervention arm compared to the whole sample in the same arm (Table 5.14).

Table 5.14: Providers' knowledge on cause and prevention of malaria (mean of cluster summaries from the 9 intervention and 9 control clusters)

Provider's knowledge of malaria cause and prevention	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Percentage who said that malaria was only caused by a parasite in a mosquito:			
Baseline	6.2 (3.0)	11.3 (12.4)	
Follow-up	6.9 (6.3)	10.3 (8.1)	3.3 (-3.9, 10.6)
Tibamal® trained outlets	-	12.1 (8.6)	
Percentage of providers mentioning one of the below as a malaria preventative measure:			
Sleeping under a net:			
Baseline	93.5 (5.4)	91.3 (6.6)	
Follow-up	94.3 (4.7)	96.4 (1.8)	2.1 (-1.5, 5.7)
Tibamal® trained outlets	-	97.5 (3.9)	
Indoor residual spraying:			
Baseline	13.9 (11.3)	15.7 (10.2)	
Follow-up	17.0 (6.4)	19.0 (12.0)	2.0 (-7.6, 11.6)
Tibamal® trained outlets	-	23.9 (13.6)	
Mosquito repellent:			
Baseline	11.6 (8.1)	11.4 (8.3)	
Follow-up	7.2 (5.7)	11.0 (6.0)	3.7 (-2.1, 9.6)
Tibamal® trained outlets	-	13.7 (8.5)	

Respondents were asked to list common symptoms they would expect to observe in a four year old child suffering from uncomplicated and complicated malaria (Table 5.15). Fever was the most commonly reported symptom of uncomplicated malaria, mentioned by an average of 67% of respondents at baseline. The number of respondents mentioning fever rose more in the intervention arm compared to the control arm, resulting in a significant difference between the means at follow-up of 9.7% points (95% CI: 2.4, 17.0). There was not much difference seen in respondents mentioning other symptoms of malaria between the arms from baseline to follow-up, except for vomiting where, although a similar percentage of respondents mentioned vomiting as a symptom at baseline, the percentage decreased in the control arm and increased in the intervention arm creating an 11.1% point (95% CI: 2.0, 22.4) difference between the means. The responses given by the sample of respondents in the intervention arm were similar to those given in the sub-sample of outlets trained on Tibamal® (Table 5.15).

Table 5.15: Providers' knowledge on symptoms of uncomplicated malaria in a four year old child (mean of cluster summaries from the 9 intervention and 9 control clusters)

Symptoms of uncomplicated malaria:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Fever:			
Baseline	66.4 (10.7)	68.1 (11.6)	
Follow-up	74.3 (8.0)	84.0 (6.5)	9.7 (2.4, 17.0)
Tibamal® trained outlets	-	87.3 (8.9)	
Sweating:			
Baseline	20.4 (21.2)	19.9 (19.7)	
Follow-up	13.7 (10.5)	12.7 (9.2)	-1.1 (-10.9, 8.8)
Tibamal® trained outlets	-	13.6 (14.7)	
Shivering:			
Baseline	28.4 (10.1)	30.5 (6.8)	
Follow-up	30.2 (11.8)	26.5 (11.0)	-3.7 (-15.1, 7.7)
Tibamal® trained outlets	-	21.2 (13.5)	
Headache:			
Baseline	45.2 (8.7)	43.7 (12.7)	
Follow-up	40.5 (8.3)	35.5 (7.7)	-5.0 (-13.0, 3.1)
Tibamal® trained outlets	-	40.6 (9.5)	
Body pain:			
Baseline	36.0 (12.0)	30.6 (9.6)	
Follow-up	39.2 (10.6)	35.1 (15.6)	-4.1 (-17.5, 9.2)
Tibamal® trained outlets		39.6 (16.2)	
Mild cough or cough:			
Baseline	7.0 (6.7)	5.9 (4.5)	
Follow-up	6.6 (4.3)	8.2 (4.8)	1.6 (-3.0, 6.2)
Tibamal® trained outlets		11.3 (8.0)	
Vomiting:			
Baseline	39.7 (5.8)	38.0 (11.1)	
Follow-up	28.4 (9.2)	40.6 (11.1)	11.1 (2.0, 22.4)
Tibamal® trained outlets		49.3 (16.0)	
Diarrhoea:			
Baseline	11.1 (10.0)	11.5 (7.5)	
Follow-up	8.4 (6.6)	10.3 (6.0)	1.9 (-4.4, 8.1)
Tibamal® trained outlets		15.1 (7.9)	
Irritability:			
Baseline	2.1 (2.5)	2.2 (2.1)	
Follow-up	4.2 (4.5)	3.7 (2.6)	-0.5 (-4.2, 3.2)
Tibamal® trained outlets		6.4 (7.8)	
Loss of appetite:			
Baseline	19.0 (9.5)	20.8 (6.7)	
Follow-up	21.5 (.10.5)	26.2 (7.2)	4.6 (-4.4, 13.7)
Tibamal® trained outlets		30.3 (8.7)	

The most mentioned symptom of complicated malaria was the child being unable to eat or drink, being mentioned by 35% and 36% of respondents at baseline in the control and intervention arm respectively; this rose to 40% in both arms at follow-up (Table 5.16). There was a 17% point increase in respondents in the intervention arm mentioning severe vomiting as a symptom from baseline to follow-up, and no change in percentage in the control arm resulting in a large 12% point (95%CI:3.5, 19.9) difference in means between the two arms at follow-up. The percentage mentioning convulsions as a symptom of complicated malaria increased by 11% points in the intervention and control arms. No significant difference was observed between the arms at follow-up for other symptoms of severe disease; responses from Tibamal® trained outlets remained relatively similar to all outlets in the intervention arm (Table 5.16).

5.2.6: Provider Knowledge of Malaria treatment

At baseline 38% of respondents in the control arm and 34% in the intervention arm were able to identify AL as the first line treatment recommended for malaria (Table 5.17). At follow-up knowledge of the first line treatment had improved in both arms, but was significantly greater in the intervention arm compared to the control arm (difference in means: 24.2% (95%CI: 14.8, 33.6) p=0.0001 (p value remaining unchanged when controlled for outlet type). Knowledge of the first line treatment was 85% in Tibamal® trained outlets, 14% points higher than the average of all outlets in the intervention arm. Respondents were asked where they would recommend a four year old suspected to be suffering from uncomplicated malaria to seek treatment first (Table 5.18). At baseline, across both arms, just over one third said they would refer the child directly to a health facility. The percentage recommending this action remained similar at follow-up in the control arm, while in the intervention arm, there was a significant 13% point decrease in the percentage that would make the same recommendation, resulting in a 19.9% point (p value=0.0003; 95% CI: 10.7, 29.1) difference at follow-up observed between the arms. At baseline just over half of respondents said they would advise the child's caregiver to buy medicine from a retail outlet.

Table 5.16: Providers' knowledge on symptoms of complicated malaria in a four year old child (mean of cluster summaries from the 9 intervention and 9 control clusters)

Symptoms of complicated malaria:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Convulsions:			
Baseline	32.2 (8.7)	33.4 (11.3)	
Follow-up	41.3 (14.5)	41.3 (10.6)	0.0 (-12.7, 12.7)
Tibamal® trained outlets	-	52.8 (12.7)	
Severe Weakness:			
Baseline	24.4 (12.0)	24.8 (12.8)	
Follow-up	33.8 (11.6)	35.8 (12.2)	2.0 (-9.9, 13.9)
Tibamal® trained outlets	-	36.6 (14.7)	
Abnormal Breathing:			
Baseline	23.9 (11.3)	24.0 (11.9)	
Follow-up	15.8 (7.7)	23.0 (6.0)	0.1 (-11.5, 11.7)
Tibamal® trained outlets	-	24.7 (15.6)	
Unconsciousness:			
Baseline	13.2 (7.0)	10.6 (5.3)	
Follow-up	10.3 (7.9)	17.0 (6.7)	6.7 (-0.6, 14.0)
Tibamal® trained outlets	-	20.1 (11.7)	
Unable to eat or drink:			
Baseline	35.1 (14.2)	36.0 (15.6)	
Follow-up	39.5 (12.7)	40.3 (13.7)	0.8 (-12.4, 14.0)
Tibamal® trained outlets	-	43.2 (16.7)	
Severe vomiting:			
Baseline	17.4 (7.6)	12.7 (7.6)	
Follow-up	17.9 (8.5)	29.6 (7.9)	11.7 (3.5, 19.9)
Tibamal® trained outlets	-	37.6 (16.0)	
Severe diarrhoea			
Baseline	6.7 (6.2)	5.4 (5.3)	
Follow-up	6.1 (3.2)	5.9 (3.2)	-0.1 (-3.4, 3.1)
Tibamal® trained outlets	-	8.8 (5.7)	

The percentage of respondents recommending this action remained similar at follow-up in the control arm but increased to 71% in the intervention arm (difference in means: 19.3%; 95% CI 9.9, 28.8). Changes observed in the intervention arm outlets were reflected in the sub-sample of Tibamal® trained outlets but were more exaggerated. No respondent said they would refer caregivers to a traditional healer (Table 5.18).

Table 5.17: Providers knowing the recommended 1st line treatment for uncomplicated malaria (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of outlets knowing the first line antimalarial for uncomplicated malaria:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)	P value[1] Adjusted *Unadjusted*
Baseline	37.8 (9.0)	34.3 (16.6)		
Follow-up	46.9 (7.6)	71.1 (10.9)	24.2 (14.8, 33.6)	0.0001 *0.0001*
Tibamal® trained outlets	-	84.8 (7.7)		-

Table 5.18: Advice on where to first seek treatment for uncomplicated malaria in a four year old child (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	39.0 (17.7)	38.0 (16.8)	
Follow-up	44.7 (10.0)	24.8 (8.4)	-19.9 (-10.7, -29.1)
Tibamal® trained outlets	-	7.4 (4.3)	
Buy medication from a retail outlet :			
Baseline	52.5 (18.2)	56.0 (19.6)	
Follow-up	51.6 (11.9)	70.9 (6.1)	19.3 (9.9, 28.8)
Tibamal® trained outlets	-	88.9 (4.3)	
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0)
Tibamal® trained outlets	-	0 (0)	
Would not know what to do:			
Baseline	4.9 (1.7)	2.6 (2.6)	
Follow-up	2.3 (2.6)	1.2 (1.8)	-1.1 (-3.3, 1.2)
Tibamal® trained outlets	-	0 (0)	
Other[1]:			
Baseline	0.7 (1.5)	0.4 (1.7)	
Follow-up	0 (0)	0.4 (1.2)	0.4 (-0.4, 1.2)
Tibamal® trained outlets	-	0 (0)	

[1] Other includes treatment at home with western medications, keeping the child warm when it is cold and maintaining good hygiene.
Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136

When it came to treating complicated malaria in children of four years, over 70% of respondents at baseline, in both arms said they would refer the child directly to a health facility (Table 5.19). This increased to 80% or more at follow-up, across the arms, and reached 91% in the sub-sample of Tibamal® trained outlets. At baseline, 16% in the control arm and

19% in the intervention arm said they would advise the child to be treated with medication from a retail outlet; at follow-up this decreased to 11% in both arms, and 8% in Tibamal® trained outlets (Table 5.19). The distance of providers from a public health facility had no significant impact on place of referral (appendix 11).

Table 5.19: Advice on where to first seek treatment for complicated malaria in a four year old child (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	74.1 (12.0)	75.9 (7.3)	
Follow-up	83.7 (6.4)	86.9 (4.0)	3.21 (-2.1, 8.6)
Tibamal® trained outlets	-	90.6 (2.5)	
Buy medication from a retail outlet:			
Baseline	16.0 (10.3)	18.6 (6.9)	
Follow-up	11.1 (5.9)	10.5 (5.0)	-0.6 (-6.1, 4.9)
Tibamal® trained outlets	-	8.0 (7.8)	
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0)
Tibamal® trained outlets	-	0 (0)	
Would not know what to do:			
Baseline	4.4 (2.3)	2.1 (3.3)	
Follow-up	4.2 (3.3)	1.8 (2.2)	-2.4 (-5.2, 0.4)
Tibamal® trained outlets	-	0 (0)	
Other[1]:			
Baseline	0.6 (1.1)	1.5 (3.2)	
Follow-up	1.5 (1.5)	1.0 (1.5)	-0.5 (-2.0, 1.0)
Tibamal® trained outlets	-	0.6 (1.8)	

[1]Other includes praying and sponging the child
Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136

5.2.7: Provider knowledge of AL dispensing practices

Respondents were asked about the advice they would give to a caregiver purchasing any brand of AL for their four year old child (Table 5.20). Respondents were asked to advise on AL administration, what to do if the child vomits, what to do if the child does not improve, and foods to administer with the medication[3]. Less than 1% of respondents at baseline were able

[3] Correct advice: AL administration: two tablets twice daily for three days with an eight hour gap between the first and second dose; Vomiting: repeat dose vomited if child vomits up to an hour after administration. Those purchasing Tibamal® should return to the outlet to get a replacement for the tablets vomited; if the child does not improve: go to the health facility. Those trained on Tibamal® were to advise the caregiver to return to the outlet for a referral form before proceeding to the health facility; Foods to administer: milk, bananas, honey and fatty foods to be given with the tablets.

to give the correct advice on AL administration, and this remained the case in the control arm at follow-up. However in the intervention arm 13% of respondents were able to give the correct advice at follow-up (difference in means 11.7%; 95% CI: 3.7, 19.8)). Similarly, advice on what to do if the child vomits was 0% at baseline in both arms, rising to 2% in the control arm at follow-up, and 9% in the intervention arm (difference in means: 7.9% (95% CI: 2.9, 12.9)). Respondents were most knowledgeable on the type of advice to give if the child does not improve, with 46% and 49% giving the correct response at baseline in the control and intervention arms respectively. This percentage remained constant in the control arm at follow-up, however in the intervention arm the percentage increased to 66% (difference in means: 26.2 (95%CI: 15.0, 37.4)). The correct advice on what foods to give the child also improved by 19% points from baseline to follow-up in the intervention arm and by 2% points in the control arm (difference in means: 21.1% (95%CI: 12.1, 30.0)). Tibamal® trained outlets were more knowledgeable in treatment advice, however only 3% in the intervention arm stated that they would tell the patient to return to the outlet to replace any Tibamal® doses that the child vomited, and only 13% would tell the caregiver to return for a referral form to go to the health facility if the child had taken Tibamal® and did not improve (Table 5.20).

5.2.8: Provider knowledge of adverse drug reactions to AL

At both baseline and follow-up, and between control and intervention arms, less than 13% of respondents were able to identify each of the possible AL ADR symptoms highlighted during the training. Tibamal® trained outlets did not perform much better than all outlets in the intervention arm (Table 5.21).

Table 5.20: Respondents giving the correct dispensing advice for AL use in a four year old child (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of respondents that knew the correct advice to give while dispensing AL concerning:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
AL administration:			
Baseline	0.7 (1.4)	0 (0)	
Follow-up	1.2 (1.5)	13.0 (11.3)	11.7 (3.7, 19.8)
Tibamal® trained outlets	-	22.5 (19.3)	
What to do if the child vomits after taking the medication:			
Baseline	0 (0)	0 (0)	
Follow-up	1.5 (2.4)	9.4 (6.7)	7.9 (2.9, 12.9)
Tibamal® trained outlets	-	18.6 (11.2)	
What to do if the child does not improve:			
Baseline	46.4 (10.0)	49.0 (12.6)	
Follow-up	39.8 (13.6)	66.0 (8.3)	26.2 (15.0, 37.4)
Tibamal® trained outlets:	-	94.0 (6.3)	
Foods to give the child with AL			
Baseline	8.3 (5.7)	8.6 (9.8)	
Follow-up	6.3 (5.9)	27.4 (11.2)	21.1 (12.1, 30.0)
Tibamal® trained outlets	-	46.8 (15.4)	

Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136
Correct advice: AL administration: two tablets twice daily for three days with an eight hour gap between the first and second dose; Vomiting: repeat dose vomited if child vomits up to an hour after administration. Those purchasing Tibamal® should return to the outlet to get a replacement for the tablets vomited; if the child does not improve: go to the health facility. Those trained on Tibamal® were to advise the caregiver to return to the outlet for a referral form before proceeding to the health facility; Foods to administer: milk, bananas, honey and fatty foods to be given with the tablets.

Around 27% to 29% of respondents at follow-up across both arms said they would refer a patient directly to a health facility if they identified symptoms of an AL ADR (Table 5.21). This increased slightly to 38% at follow-up in the control arm and 45% in the intervention arm (no significant difference between arms, p value= 0.1535 (difference in means 7.7%; 95%CI: -3.2, 18.5). An average of 13% of respondents across both arms and time points said that they had observed what they thought was an ADR to AL. Of those who said they had observed an ADR, 35% and 52% at baseline in the control and intervention arm respectively reported to have referred patients directly to a health facility. At follow-up the percentages were similar in the two arms at 33% and 35% in the control and intervention arms respectively (p value=0.8982) (difference in means: 1.8%; 95% CI: -27.8, 31.4). AL ADR referral practices of Tibamal® trained outlets were similar to all outlets in the intervention arm (Table 5.22).

Table 5.21: Percentage of respondents knowing AL ADR symptoms (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of outlets that can identify symptoms of suspected AL/ Tibamal® ADRs	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Nausea:			
Baseline	11.2 (7.45)	9.8 (8.8)	
Follow-up	7.6 (7.5)	6.4 (6.3)	-1.1 (-8.0, 5.7)
Tibamal® trained outlets	-	8.9 (14.2)	
Vomiting:			
Baseline	11.3 (8.6)	11.1 (7.9)	
Follow-up	6.4 (7.0)	6.1 (5.1)	-0.3 (-6.4, 5.8)
Tibamal® trained outlets	-	7.6 (7.1)	
Diarrhoea:			
Baseline	4.8 (7.3)	4.8 (6.4)	
Follow-up	2.1 (2.7)	1.6 (2.2)	-0.4 (-2.9, 2.1)
Tibamal® trained outlets	-	2.2 (3.4)	
Dizziness:			
Baseline	12.6 (9.0)	7.5 (6.2)	
Follow-up	12.9 (11.8)	11.8 (9.6)	-4.9 (-15.7, 5.9)
Tibamal® trained outlets	-	11.7 (13.6)	
Skin rash:			
Baseline	4.5 (5.0)	2.9 (2.9)	
Follow-up	5.3 (3.8)	9.2 (6.0)	3.9 (-1.2, 8.9)
Tibamal® trained outlets	-	2.2 (3.4)	
Itching/ scratching:			
Baseline	7.4 (5.1)	8.3 (5.6)	
Follow-up	5.7 (2.8)	10.5 (5.0)	4.8 (0.7, 8.9)
Tibamal® trained outlets	-	14.8 (8.3)	

Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136

Outlets were supplied with CHW referral forms by PSI. These were to be filled out for each suspected ADR or failed treatment with AL and taken by the patient to the facility. A copy was to remain in the outlet to be collected by one of the PSI sales staff and sent to the Pharmacy and Poisons Board. 40% of outlets at follow-up in the intervention arm had CHW referral forms and 19% of outlets said they had filled in a form during the past one month (Table 5.23). Around 2% of outlets in the control arm reported having referral forms of which half said they had filled a form in within the past month. 78% of Tibamal® trained outlets in the intervention arm had referral forms of which 18% had been filled in within the past month. Although 19% of 125 outlets with CHW forms said they had filled in a referral form within the past month only one filled in form was received by PSI/ PPB over the 8 months that Tibamal® drug distribution was on-going. CHW referral forms are also used outside of the Tibamal® study by Child and Family Wellness Clinics and also CHWs who may also own or work in drug shops. From the data available, it was not possible to distinguish forms from the study and those from other sources. Also, since it seems a large proportion of the forms did not reach the PPB, it is not possible to identify the proportion of forms filled in that represented ADRs and those that represented treatment failures.

Table 5.22: Respondents' referral practices for suspected AL ADRs (mean of cluster summaries from the 9 intervention and 9 control clusters)

Referral practices for suspected AL ADRs:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95%CI)
Percentage of outlets that would immediately refer patients to a health facility for a suspected ADR*:			
Baseline	27.1 (10.6)	29.3 (10.1)	
Follow-up	37.5 (9.3)	45.2 (12.2)	7.7 (-3.2, 18.5)
Tibamal® trained outlets	-	55.0 (11.3	
Percentage of outlets that had observed a suspected AL ADR[1]:			
Baseline	13.2 (8.7) 27	13.6 (11.2) 23	
Follow-up	11.6 (9.6) 36	11.4 (4.6) 35	-0.2 (-7.7, 7.3)
Tibamal® trained outlets	-	20.4 (9.6)	
Of those observing a suspected AL ADR: percentage that referred a suspected AL ADR directly to a health facility:			
Baseline	32.1 (34.0)[2]	52.4 (31.1)[1]	
Follow-up	32.9 (29.1)[1]	34.7 (26.0)	1.8 (-27.8, 31.4)
Tibamal® trained outlets		32.4 (22.2)	

[1] cluster summaries from 7 clusters; [2] cluster summaries from 8 clusters; Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136

Table 5.23: Respondents' use of CHW referral forms at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

CHW referral forms:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95%CI)	P value Unadjusted Adjusted
Percentage of outlets with CHW forms:	2.2 (1.7) 7	39.6 (14.2) 125	37.4 (27.2, 47.5)	0.0001 *0.0001*
Tibamal® trained outlets	-	78.0 (15.5) 110		-
Of which:			-	-
Percentage of outlets that had filled in a CHW form in the past month	50.0 (54.8)[1]	19.8 (12.6)		
Tibamal® trained outlets		18.2 (15.9)		

[1] cluster summary from 6 clusters; Denominators: refer to table 5.3; Tibamal® trained outlets: control=3, intervention=136

5.2.9: Factors influencing antimalarial stocking and selling practices

The five most common factors determining which antimalarials to stock at follow-up are shown in Figure 5.5 (interviewees could specify more than one factor). By far the most frequently cited factor in both arms was customer demand, mentioned by 90% and 82% in the control and intervention arm respectively. The next most common factors mentioned were MOH recommendations and affordability. The percentage mentioning the importance of the medication being recommended by the MOH was almost twice as high in the intervention group than in the control (21% and 11% respectively). The need for the drug to be affordable to the provider was mentioned by 31% of respondents in the control arm and 19% in the intervention arm, while the influence of PSI staff on what to stock was only mentioned in the intervention arm by 12% of respondents. In Tibamal® trained outlets, customer demand was also mentioned the most, followed by the influence of the MOH (30%) and PSI sales staff (20%) (Figure 5.5).

Figure 5.6 displays the five most mentioned factors influencing which antimalarial a retailer will sell to a customer, if the outlet usually stocked more than one antimalarial. The percentage of responses remained similar at baseline and follow-up for each factor. The most common influence was again customer demand, mentioned by 65% and 66% of respondents in the control and intervention arm respectively. In Tibamal® trained outlets, customer demand was also the most commonly mentioned (65%). If a customer came to buy antimalarials from an outlet and did not have enough money, 63% of respondents in the control arm and 71% in the intervention arm said they would give the antimalarial to the customer on credit; credit was more likely to be given if the respondent knew the customer (Figure 5.7). Around one third of respondents in both arms said they would refuse to sell the medication to the customer. Less than 20% said they would refer the customer elsewhere (for example to a health facility where treatment should be free); offer cheaper alternatives, or sell part of a full dose. Responses given by Tibamal® trained outlets were similar to those of all outlets in the intervention arm (Figure 5.7).

Figure 5.5: Factors influencing which antimalarials to stock at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

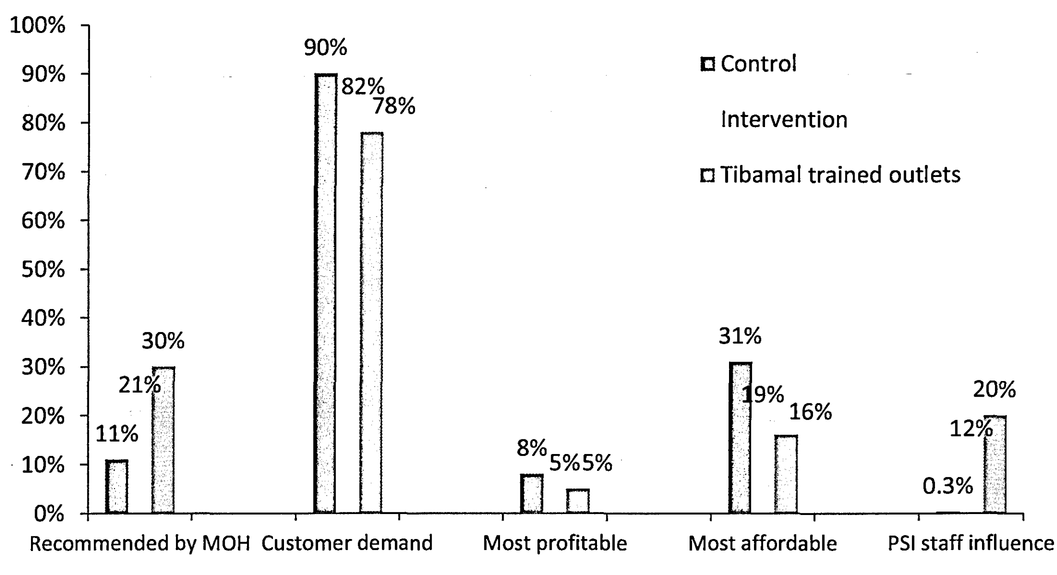


Figure 5.6: Factors influencing which antimalarials to sell, if more than one antimalarial is available, at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

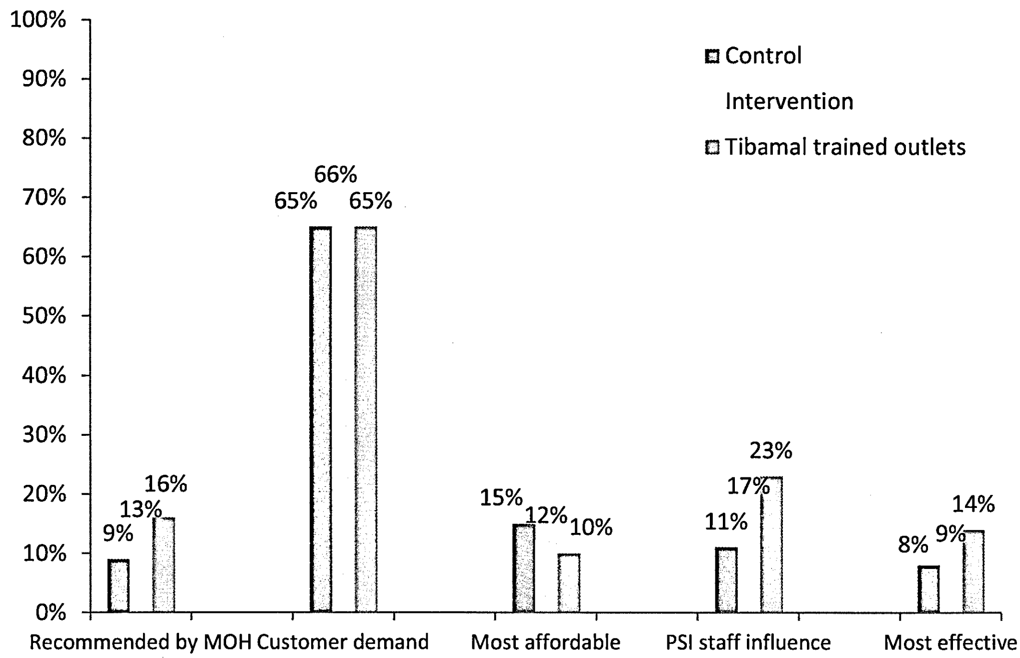
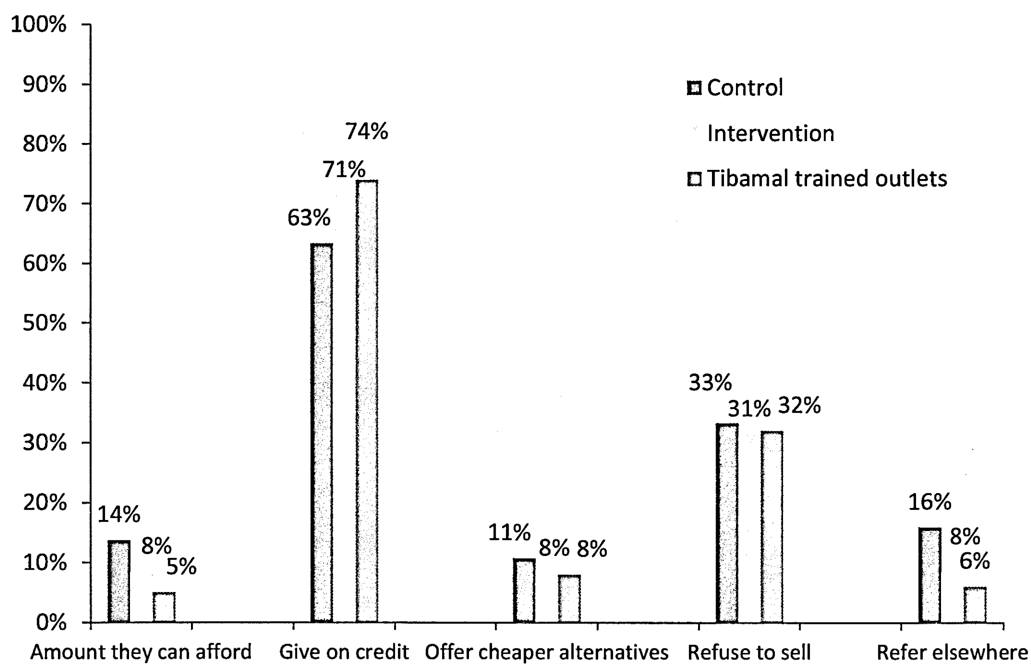


Figure 5.7: Actions respondents take if customer has insufficient funds, at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)



5.3: DISCUSSION

Exposure of the control arm population to the intervention ("contamination") was minimal, with only one control respondent saying that they had attended the Tibamal® training and usually sold Tibamal® (though they had none in stock on the day of the survey), and only 14% having heard of Tibamal®.

However, several other limitations should be borne in mind when interpreting the study findings. It is well known that there is often a difference between provider knowledge and provider behaviour. Therefore the percentage correctly answering questions on areas such as counselling advice should be considered as the upper bound of those actually providing such advice to consumers. There is also generally a gap between reported and actual behaviour, reflecting social desirability bias i.e. the respondents aim to present themselves in a favourable light to the survey team. This may lead them to for example under-report the frequency with which they would sell under-doses to caregivers with insufficient funds, or to report lower than actual retail drug prices. It will be possible to investigate these issues further by comparing the provider survey data with that obtained from the mystery shopper activity (Chapter 6). Stock outs were assessed by asking providers if they had experienced any stock outs of AL over the past two weeks prior to the survey. Since very few outlets keep any documentation of their stocks, the recall period was limited to the previous two weeks to minimise re-call bias. Only outlets that currently had stocks of AL were asked about the duration of any past stock outs, as they were therefore able to provide a definite end date of any stock-outs. This may have underestimated the real duration of stock outs since outlets currently out of stock were excluded from the analysis and they could have been the outlets that had suffered from the longest duration of stock-outs.

Shops that had undergone Tibamal® training were identified by asking the respondent if any of the staff had attended the training. There may have been some respondents that wrongly informed us that no staff had attended the training either because of recall bias or because they were not aware that anyone did attend the training. However the differences observed in responses given from Tibamal® trained outlets to all outlets in the intervention arm (trained or not) do indicate that most Tibamal® trained outlets were correctly identified. The intervention improved access to AL treatment by significantly increasing the availability of AL in retail outlets to 37% in the intervention arm compared with 5% in the control, and decreasing its median cost by around 9 shillings per tablet (0.11 USD). This is equivalent to a 12 pack dose given to children 3 to 7 years costing 40 KSH (0.48 USD) instead of 151 KSH (1.86 USD) and an adult's 24 pack dose costing 79 KSH (0.97 USD) instead of 300 KSH (3.69 USD). Providers also became more knowledgeable on how to treat uncomplicated malaria with 71% in the intervention arm compared to 47% in the control arm knowing the government recommendation for the first line drug. Tibamal® was also seen as effective, with the vast majority of intervention respondents at follow-up reporting it to be more effective than other antimalarials. The findings from this survey also show the key importance of consumer demand in determining what drugs are stocked and sold to customers, and indicate that the Tibamal® community awareness activities were also likely to have made an important contribution to provider awareness. Slightly worrying is that a percentage of providers, albeit small (<5% in Tibamal® trained outlets) were willing to sell customers less than the recommended dose of treatment if the customer had insufficient funds. Patients taking less than the recommended dose of AL treatment reduces levels of adherence and is a potential factor for increasing drug selection pressure and hence parasite resistance to the treatment. Ideally no provider should sell insufficient doses to customers. This is something that needs to be reinforced in training and follow-up supervision, and providers should be made aware of the negative effects of such practices.

The finding that only slightly over one third of outlets in the intervention arm stocked AL at follow-up reflects the fact that not all retailers were eligible or willing to stock Tibamal®. The subsidised drug should only have been stocked by those who had attended the Tibamal® training (i.e. 43% of intervention outlets). The remaining 57% of outlets were not trained for a number of reasons. Outlets selected for training were identified during the baseline retail census and had to have been functioning for a minimum period of six months and have been selling an anti-malarial or anti-pyretic within the past year. Some new outlets were added to the sample frame at follow-up that met the criterion of being established for at least 6 months, but would not have been eligible for Tibamal® training at baseline. Also as businesses sometimes change the type of business they run, outlets previously never selling medication may have decided to do so between the two study time points, but would not have met the training criteria at baseline. In addition, some outlets identified for inclusion were unable to attend the training due to other commitments; and some outlets may have been closed when invitations to attend training were being given. Even after receiving training some outlets may have changed the type of business they were running and stopped selling medication, closed up their business, or relocated to outside the study area. These issues highlight the challenges of maintaining a trained cadre of retailers in such a dynamic market.

All trained shops were given the option of stocking AL but not all opted for this, mainly because they did not have sufficient funds to purchase AL from the PSI sales staff (personal communication Mbogo Mbunyi, PSI). On the other hand 15 intervention outlets stocked Tibamal® even though none of the staff were reported to have attended the Tibamal® training. It was not clear whether this was because the staff member who had attended training was not present on the day of survey and other staff were not aware that they had attended, whether this indicated that some untrained shops were selling the subsidised drug, or whether the trained staff were no longer working in the outlet.

There was low availability artemisinin monotherapies in the retail outlets. This was not likely to be as a result of the intervention since stocks were low both at baseline and follow-up and in both arms. Further enquiry of this observation from FGDs with shopkeepers revealed that one of the reasons for this is the high cost of these treatments making it unaffordable for both retailers to purchase them from wholesalers and for consumers (Kedenge, 2011).

Storage of AL was generally good in shops. However, at follow-up 33% of intervention outlets reported a stockout of at least one AL pack in the past 2 weeks, indicating that consistent availability of all pack sizes could be problematic.

Providers' knowledge of causes and prevention of malaria did not change post-intervention. However, in intervention areas providers were significantly more aware that fever was an important symptom of uncomplicated malaria. Knowledge of the symptoms of complicated malaria did not change post-intervention with the exception of severe vomiting.

There were significant improvements observed in the knowledge of counselling advice when selling AL in the intervention arm compared to the control arm, especially in the Tibamal® trained outlets. However, with the exception of advice on what to do if the child does not improve, overall the percentages remained low. Of particular concern was the low percentage knowing the correct dosing for AL. These results reflect in part the partial coverage of training described above, but may also indicate poor understanding of these concepts in training, or the 9 month gap between training and the follow-up survey. During FGDs one of the providers commenting on this observation stated '*those that were trained the first time could have forgotten some of the information; because it was a one day training, and they probably did not get time to go over the notes that they were given, so they only give the advice that they remember and leave the rest that they have forgotten'.* Another factor possibly contributing to this is the low percentage of trained outlets that had Tibamal® job aids. These jobs aids contained dosing advice and were designed to support the provider in correctly dispensing AL/ Tibamal®. No reasons were given as to why so few outlets contained job aids.

Knowledge of the symptoms of AL ADRs remained low post-intervention, not reaching 15% for any individual symptom. Although at follow-up over 80% of providers in both arms knew to refer children directly to a health care facility to treat complicated malaria, this was not the case for children suffering from potential ADRs, with less than half in both arms saying they would refer the child directly to a health facility. The utility of the CHW referral forms remains questionable since many patients may not return to the retailer if they have ADR symptoms. From these data, it is not clear from the 40% of outlets with CHW forms how many had them supplied by the PSI sales staff and how many had them supplied from elsewhere, nor is it clear how many of the referrals were due to AL adverse events or treatment failure.

Summary: The intervention was successful in significantly improving access to AL treatment by increasing the availability of AL in retail outlets, improving the affordability of the treatment and increasing the percentage of providers knowing the government recommendation for the first line treatment of uncomplicated malaria. However, the intervention was not as successful in improving provider's knowledge of causes and prevention of malaria; knowledge of AL counselling advice (except on what to do if the child does not improve), and knowledge of symptoms of AL adverse drug reactions. A very low percentage of providers reported having used the CHW forms. The provider survey mainly focused on how the intervention was able to improve provider knowledge on appropriate standards of quality for the treatment of fever in children under five. The following chapter

(Chapter 6) presents the mystery shopper survey, which was used to assess whether the intervention was able to improve provider behavior when selling drugs.

REFRENCES

Kedenge S (2011) The Impact of Retail Sector Delivery of Artemether-Lumefantrine in Malaria Treatment of Children Under Five in Kenya, Focus Group Discussions. Unpublished report. KEMRI Wellcome Trust Research Programme

CHAPTER 6

MYSTERY SHOPPER SURVEY

6.1: INTRODUCTION

This chapter reports the results of the mystery shopper survey of drug outlets. The purpose of this study was to analyse the patient provider interaction to give better information on actual rather than self-reported provider behaviour, contributing to the second specific objective of the thesis: To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years. The mystery shopper survey took place a month after the retail census, at baseline and follow-up. Field workers, disguised as local residents visited selected outlets seeking treatment for a four year old child with fever. The fieldworkers presented the following scenario: *a 4 year old child (weighing 15kg) under their care who has been suffering from a recurring fever for 3 days, especially at night. The child had no other symptoms, and no medication had been given to the child so far.* The field worker was then to wait for the provider to ask further questions and/ or prescribe a medication. If no medicine was recommended, field workers were to prompt the provider to recommend a medicine. If after prompting no medicine was recommended then the field worker was instructed to find out reasons as to why. If a medicine was recommended then the field worker was to find out why the provider suggested that particular medicine. Details of the interview were discretely filled in structured questionnaires away from the outlet, once the interview was completed. As with the provider survey, outlets were included in the mystery shopper survey sample if they had been functioning for a minimum period of six months prior to the start of the retail census and had been selling either antimalarials or antipyretics within the past year. Mystery shoppers interacted with whichever retailer was present at the time of the survey. Written consent for the mystery shopper survey was obtained during the retail census carried out two months prior to the mystery shopper visits, from the provider present at that time in the outlet. Full details of the methods for the mystery shopper survey are presented in Chapter 4.

The results are presented in section 6.2. Section 6.2.1 describes the characteristics of the outlets interviewed. Section 6.2 looks at what signs and symptoms providers enquired about before making a diagnosis and prescribing treatment. Section 6.3 onwards looks at the percentage of providers who dispensed an antimalarial, and in particular AL. For those outlets that did dispense AL, these sections further analyse the type of advice given on how to take the AL and the amount paid for AL by the mystery shopper.

6.2: RESULTS

6.2.1: Outlet characteristics

During the retail censuses, a total of 600 outlets were identified at baseline and 818 at follow-up, selling an anti-malarial, an anti-pyretic or both. Of these, only outlets that had been reported to be functioning for 6 months or more were included in the sampling frame for the survey comprising 295 and 225 outlets in the control and intervention arms respectively at baseline and 369 and 351 respectively at follow-up (Table 6.1). A total of 499 outlets were successfully interviewed at baseline, 284 and 215 in control and intervention arms respectively, and 653 outlets at follow-up, 336 in the control and 317 in the intervention arm. These numbers form the denominator for other tables and figures in this chapter. Both at baseline and follow-up, over 90% of the outlets sampled were successfully interviewed, with the majority (over 70%) of outlets interviewed being general stores (Table 6.2). During the provider survey described in Chapter 5, retailers were asked for details on outlet staffing and training of employees. The characteristics of the outlets and staff surveyed for the mystery shopper survey remained similar to those of the provider survey (see Chapter 5).

Table 6.1: Outlets included in the mystery shopper survey

	Baseline		Follow-up	
	Control n (%)	Intervention n (%)	Control n (%)	Intervention n (%)
Outlets sampled	295	225	369	351
Outlets interviewed[1]	284/295 (96.3)	215/225 (95.6)	336/369 (91.1)	317/351 (90.3)

[1]Reasons for an outlet not being interviewed included: temporary closure, permanent closure, change of type of business, moving location, declining to be interviewed for the mystery shopper survey at the time of the retail census or duplication during the retail census.

Table 6.2: Distribution of outlets successfully interviewed, by type (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Baseline		Follow-up	
	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n
Specialized drug stores[1]	17.9 (10.0) 48	25.0 (13.7) 55	17.3 (8.6) 58	22.0 (8.2) 71
General stores	82.1 (10.0) 236	74.6 (14.0) 159	82.7 (8.6) 278	77.9 (8.2) 246
Other outlet type[2]	0.0 (0) 0	0.4 (1.3) 1	0.0 (0) 0	0.0 (0) 0

[1] Specialized drug stores included: pharmacies, chemists, drug shops, clinics with over the counter services, Bamako Initiative (BI) outlets and Child and Family Wellness Clinics.
[2] Other outlet type= an agro vet shop

6.2.2: Asking about signs of severe disease

To determine need for referral of a child to a health facility, retailers were expected to ask about various symptoms that the child could be experiencing. As per the retailer training, these signs included: inability to eat, drink or breastfeed, convulsions, severe weakness, unconsciousness (coma), abnormal breathing, severe vomiting and severe diarrhoea. At baseline, staff at 27% of outlets in the control arm and 22% in the intervention arm asked whether the child had at least one of these signs of severe disease. At follow-up there was a slight increase (12% points) in the intervention arm to 33% for all outlets. There was a 19% point increase in the intervention arm for general stores from 11% at baseline to 30% at follow-up but a 17% point fall from 55% to 38% in specialized drug stores. There was no evidence of a significant difference between the control and intervention arms at follow-up (unadjusted p=0.4295; adjusted p=0.3824). On average about 45% of outlets with staff with clinically related training asked about at least one severe sign at baseline and about 35% at follow-up across both arms (Table 6.3). In the intervention arm at follow-up, 41% of outlets with staff with Tibamal® training, compared to 22% of those without Tibamal® training asked about signs of severe disease.

Table 6.3: Percentage of outlets where retailers asked whether the child had at least one sign of severe disease (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	P-value[1] Unadjusted *Adjusted*
All outlets:				
Baseline	26.5 (14.1)	21.6 (12.4)		
Follow-up	27.4 (10.7)	33.3 (14.2)	5.9 (17.7, -7.9)	0.4295[3] *0.2667*
By outlet type:				
Specialized drug stores:				
Baseline	50.2 (29.9)	55.1 (15.2)		
Follow-up	37.2 (18.1)	37.8 (25.0)	0.6 (22.4, -21.2)	
General stores:				
Baseline	21.6 (12.7)	11.0 (9.2)		
Follow-up	24.4 (12.8)	30.1 (17.9)	5.6 (21.2, -9.9)	
By whether any staff have clinically-related training[2]:				
Outlets with clinically-related training:				
Baseline	47.5 (28.6)	44.8 (29.7)		
Follow-up	34.5 (25.4)	37.4 (31.1)	2.9 (31.3, -25.5)	
Outlets without clinically-related training:				
Baseline	22.0 (13.2)	15.9 (9.9)		
Follow-up	26.3 (14.7)	29.5 (18.6)	3.3 (20.0, -13.5)	

[1] P-value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.
[2] Information based on outlets interviewed both for mystery shopper and provider survey.
[3]Difference in difference analysis, unadjusted p value=0.2283 (*appendix 12*)

6.2.3: Drugs dispensed, reasons for not dispensing and referral advice

Tables 6.4-6.6 show the various drugs dispensed by the retailers and reasons given by outlets that did not dispense drugs. Tables 6.7 & 6.8 show referral advice given by retailers and specifically by outlet type. Tables 6.9 & 6.10 give similar details of drugs dispensed comparing specialized drug stores and general stores. 70% and 60% of outlets visited at baseline and follow-up respectively dispensed drugs to mystery shoppers. Retailers that dispensed drugs dispensed antipyretics, antimalarials and other drugs including antibiotics, anti-histamines, antihelminthics and bronchodilators (see footnote to Table 6.9 for details of specific drugs). At baseline, 44% in the control and 29% in the intervention arm sold an anti-pyretic on its own. At follow-up, there was a significant 17% point difference between arms for this indicator (unadjusted p=0.0074; adjusted p=0.0175), with 36% of outlets in the control and 19% in the intervention arm dispensing an anti-pyretic on its own. At baseline 25% of outlets in the control arm and 41% in the intervention arm, dispensed antimalarials, which was fairly similar at follow-up with 20% of outlets in the control and 40% in the intervention arm dispensing an antimalarial (Table 6.4). The difference between arms at baseline was 16% points and 20% points at follow-up.

Table 6.4: Drugs dispensed by retailers (mean of cluster summaries from the 9 intervention and 9 control clusters)

Type of drugs dispensed:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	P-value[1] Unadjusted Adjusted
Any drug:				
Baseline	69.6 (10.0)	69.4 (8.2)		
Follow-up	56.8 (6.1)	59.7 (6.9)	-2.9 (-3.6, 9.3)	0.3651 0.9116
Type of drugs dispensed Anti-pyretic alone:				
Baseline	43.6 (13.3)	28.7 (9.1)		
Follow-up	35.7 (7.7)	18.6 (5.3)	-17.1 (-10.5, -23.7)	0.0074 0.0203
Anti-pyretic with anti-malarial:				
Baseline	20.2 (7.5)	26.9 (8.0)		
Follow-up	15.1 (3.6)	23.4 (7.3)	8.3 (14.0, 25.7)	0.5808 0.1317
Any anti-malarial				
Baseline	25.2 (8.9)	40.7 (9.3)		
Follow-up	20.2 (3.7)	40.3 (6.5)	20.1 (25.4, 14.8)	<0.0001 0.0260

[1] P-value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.

The reasons for this difference between arms at baseline are not clear. However, the difference at follow-up was significant, even controlling for the baseline values (unadjusted p=<0.0001; adjusted p=0.0260), possibly due to an increase in antimalarials in the intervention arm at follow-up, likely attributable to the presence of Tibamal® in the intervention outlets.

About 90% and 50% of specialised drug stores and general stores, respectively, dispensed drugs. The proportion of outlets dispensing any anti-malarial remained fairly similar in the specialised drug stores but a 21% point difference was seen in the general stores between control and intervention arms at follow-up (Table 6.5).

Table 6.5: Drugs dispensed, by outlet type (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Specialised drug stores			General stores		
Type of drugs dispensed:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95% CI)	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95% CI)
Any drug:						
Baseline	95.6 (9.1)	88.6 (17.3)		64.0 (11.1)	58.6 (17.0)	
Follow-up	97.1 (6.0)	89.0 (11.9)	8.2 (-17.6, 1.2)	48.1 (8.8)	51.6 (5.7)	-3.6 (3.8, -11.0)
Anti-pyretic alone:						
Baseline	15.0 (16.4)	7.5 (12.1)		50.2 (14.4)	35.3 (12.1)	
Follow-up	18.1 (19.2)	13.6 (19.7)	-4.5 (14.9, -24.0)	38.5 (9.9)	21.3 (8.4)	-17.2 (-8.0, -26.4)
Anti-pyretic with anti-malarial:						
Baseline	63.6 (30.0)	68.8 (13.8)		11.4 (7.9)	11.3 (8.2)	
Follow-up	55.4 (11.6)	58.6 (25.0)	3.2 (22.6, -16.3)	6.5 (3.6)	11.9 (5.3)	5.4 (9.9, 0.9)
Any anti-malarial:						
Baseline	79.5 (23.5)	79.6 (15.7)		13.4 (8.7)	24.0 (17.9)	
Follow-up	75.1 (20.1)	72.6 (24.8)	-2.5 (20.1, -25.1)	9.3 (4.3)	29.9 (8.4)	20.6 (27.3, 14.0)

In outlets where retailers did not dispense any drugs, the main reasons given were referral to a specialised drug store or health facility. A significant difference (17% points) was seen at follow-up in referral to a health facility (unadjusted p=0.0339; adjusted p=0.0103) with intervention outlets being less likely to refer (Table 6.6). Other reasons given for not dispensing drugs included: lack of drugs in stock, lack of antimalarials in stock, and lack of suitable drugs to treat a child.

Table 6.6: Of those retailers not dispensing any drugs, reasons given for not dispensing (mean of cluster summaries from the 9 intervention and 9 control clusters) (multiple responses allowed)

Reasons for not dispensing any drug:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	P-value[1, 3] Unadjusted *Adjusted*
No drugs in stock:				
Baseline	19.8 (19.0)	36.8 (24.2)		
Follow-up	30.7 (12.6)	20.3 (7.9)	-10.4 (0.2, -20.9)	0.0531 *0.0308*
No antimalarials in stock:				
Baseline	8.0 (11.2)	7.3 (9.0)		
Follow-up	18.1 (14.3)	31.1 (16.3)	13.0 (28.3, -2.3)	0.0915 *0.1145*
No suitable drugs in stock[2]:				
Baseline	19.7 (15.2)	21.8 (15.2)		
Follow-up	33.7 (13.7)	35.5 (16.9)	1.8 (17.2, -13.6)	0.8061 *0.6892*
Referred to a specialized drug store:				
Baseline	72.4 (23.2)	67.6 (20.0)		
Follow-up	75.3 (17.6)	72.0 (19.9)	-3.3 (15.6, -22.1)	0.7188 *0.4017*
Referred to a health facility:				
Baseline	33.4 (25.9)	29.2 (23.5)		
Follow-up	38.2 (21.1)	21.6 (4.5)	-16.7 (-1.4, -31.9)	0.0339 *0.0109*

[1] P-value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.

[2] Shopkeeper said they had no suitable drugs in stock which generally meant that either they did not feel they had appropriate drugs to treat the stated symptoms, or that they did not have appropriate drugs to treat children of the stated age (4 years)

[3] Difference in difference analysis: unadjusted p values for the difference in difference analysis gave similar results to those in table 6.6 apart from '*no antimalarials in stock*' and '*referred to a health facility*', where the difference in difference unadjusted p values were 0.0343 and 0.2979, respectively (*appendix 12*).

In terms of all outlets, at baseline, 7.8% of control outlets and 6.4% of intervention outlets referred patients directly to a health facility without dispensing any drugs or offering any other suggestions for treatment. At follow-up, significantly fewer outlets in the intervention arm referred mystery shoppers directly to the health facility (unadjusted p=0.0416; adjusted p=0.0119) compared to the control (Table 6.7).

Table 6.7: Percentage of retailers referring mystery shoppers to health facilities (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of referrals:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	P-value[1] Unadjusted *Adjusted*
Direct referral to health facility (no drugs dispensed or other option suggested):				
Baseline	7.8 (7.9)	6.4 (5.7)		
Follow-up	9.4 (6.7)	4.0 (3.2)	-5.5 (-0.2, -10.7)	0.0416 *0.0119*
Drugs given with referral to health facility:				
Baseline	27.1 (9.9)	22.3 (12.7)		
Follow-up	19.1 (11.5)	14.5 (3.4)	-4.6 (3.8, -13.1)	0.2632 *0.1768*

[1] P-value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.

None of the specialized drug stores at follow-up in either arm referred the mystery shoppers directly to a health facility. In the general stores at follow-up, however, there was a 6% point difference between arms with 11% and 5% of outlets in the control and intervention arms, respectively, referring the mystery shoppers directly to a health facility (Table 6.8).

Sales of AL at baseline were minimal at 0.5% in the control arm and zero in the intervention arm. At follow-up, in the control arm, sales of AL remained low at about 2% but rose significantly to 25% in the intervention arm, a difference of 24% points between arms (unadjusted p=<0.0001; adjusted p=<0.0001) (Table 6.9). Of those outlets dispensing an anti-malarial in the intervention arm, the share of AL dispensed rose markedly from 0% at baseline to 61% at follow-up (Figure 6.1). Notably, sales of amodiaquine dropped from 18% of outlets at baseline to 7% at follow-up in the control arm, and 27% to 3% in the intervention arm (Table 6.10), and there was a 55% point drop in amodiaquine's share of antimalarials dispensed in the intervention arm from baseline to follow-up (Figure 6.1). This is possibly due to the cessation of production of one of the main amodiaquine brands (Malaratab®) communicated to the survey team after baseline, by the production company.

Table 6.8: Percentage of retailers referring mystery shoppers to health facilities, by outlet type (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Specialised drug stores			General stores		
Percentage of referrals:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)
Referral to a health facility (no drugs dispensed or other option suggested):						
Baseline	0.0 (0)	7.3 (17.5)		9.2 (9.1)	7.6 (6.4)	
Follow-up	0.0 (0)	0.0 (0)	0.0 (0)	11.0 (7.4)	4.9 (3.8)	-6.1 (-2.1, -12.0)
Drugs given with referral to a health facility:						
Baseline	18.8 (15.7)	21.6 (15.3)		28.1 (11.1)	21.2 (16.7)	
Follow-up	17.2 (19.4)	19.8 (10.0)	2.6 (18.0, -12.8)	19.0 (11.7)	13.5 (3.8)	-5.5 (3.2, -14.2)

To further explore the possible reasons for not dispensing AL, I looked at the frequency of AL dispensing among only those outlets with any antimalarials and among those specifically with AL in stock at the time of the provider survey. As provider surveys were carried out approximately two weeks after the mystery shopper survey it is possible that there were some changes in stock between the two, but these were not likely to be major. Of those that had an anti-malarial in stock during the provider survey at follow-up, 5% dispensed AL in the control arm and 41% in the intervention arm. Of those that had AL in stock during the provider survey, 21% and 57% of outlets in the control and intervention arms respectively, dispensed

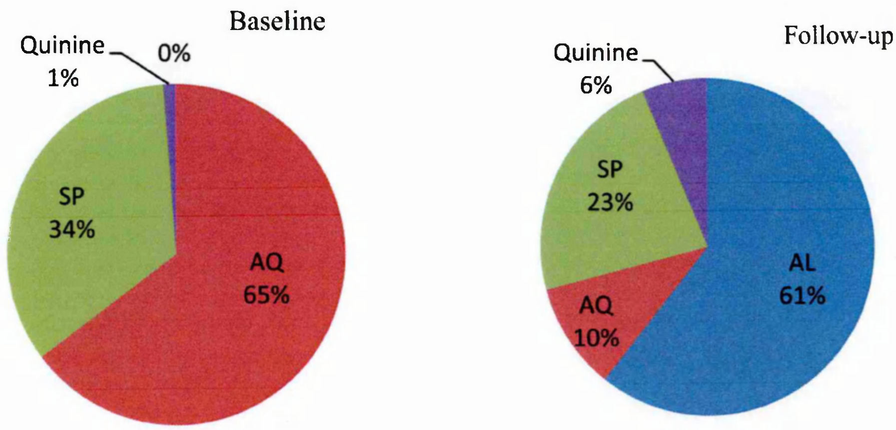
AL at follow-up to the mystery shoppers. In the intervention arm at follow-up, of the outlets with Tibamal® in stock during the provider survey, 58% dispensed Tibamal® to mystery shoppers.

Table 6.9: Specific antimalarials dispensed by retailers (mean of cluster summaries from the 9 intervention and 9 control clusters)

Anitmalarials dispensed:		Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	P-value[1, 4] Unadjusted *Adjusted*
AL[3]:					
	Baseline	0.5 (1.6)	0.0 (0)		
	Follow-up	1.8 (1.3)	25.4 (6.9)	23.6 (28.6, 18.7)	<0.0001 *<0.0001*
Tibamal®:					
	Baseline	0.0 (0)	0.0 (0)		
	Follow-up	0.0 (0)	24.4 (7.0)	24.4 (29.3, 19.5)	<0.0001 *<0.0001*
Amodiaquine:					
	Baseline	18.8 (5.6)	27.5 (13.6)		
	Follow-up	7.1 (4.9)	3.9 (4.1)	-3.2 (1.3, -7.7)	0.1502 *0.0670*
SP:					
	Baseline	6.1 (4.8)	13.8 (8.8)		
	Follow-up	9.2 (6.3)	8.8 (4.7)	-0.4 (5.1, -6.0)	0.8713 *0.5884*
Quinine:					
	Baseline	0.2 (0.6)	0.4 (1.1)		
	Follow-up	2.1 (2.4)	2.2 (2.8)	0.1 (2.7, -2.5)	0.9196 *0.9300*
Other drugs[2]:					
	Baseline	1.6 (2.8)	1.4 (2.8)		
	Follow-up	2.0 (2.5)	1.6 (2.4)	-0.4 (2.1,- 2.9)	0.7309 *0.5732*

[1] P-value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.
[2] Other drugs are non-antimalarials and non-antipyretics and include: Antibiotics (Amoxicillin, Cotrimoxazole and Trimethoprim), Antihistamines (Chlorpheniramine), Antihelminthics (Levamisole), and Bronchodilators (Salbutamol).
[3] Rank sum test: unadjusted analysis, p=0.0003; adjusted analysis, p=0.0003. This test was carried out on the main outcome indicator because of its robustness and its sensitivity to any shifts in distribution between control and intervention clusters. (Hayes & Moulton, 2009)
[4]Difference in difference analysis gave similar unadjusted p values to all indicators reported in table 6.9 (appendix 12)

Figure 6.1: Share of specific antimalarials dispensed, by outlets that dispensed an anti-malarial in the intervention arm



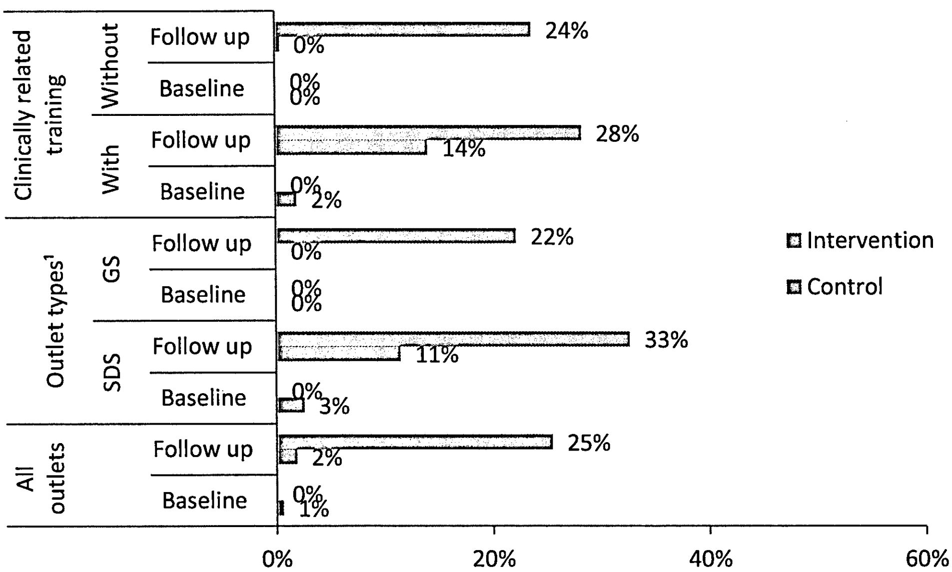
Sales of AL at follow-up were 21% points higher in the intervention arm than in the control arm for specialized drug stores and 22% higher for general stores (Table 6.10 & Figure 6.2). No Tibamal® was dispensed at baseline. At follow-up, none was dispensed in the control arm; in the intervention arm, 24% of all outlets dispensed Tibamal® (Table 6.9), 31% of specialized drug stores and 22% of general stores (Table 6.10).

Table 6.10: Specific antimalarials dispensed, by outlet type (mean of cluster summaries from the 9 intervention and 9 control clusters)

		Specialised drug stores			General stores	
Anitmalarials dispensed:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)
AL:						
Baseline	2.5 (7.4)	0.0 (0)		0.0 (0)	0.0 (0)	
Follow-up	11.4 (10.1)	32.6 (25.9)	21.2 (40.9, 1.6)	0.0 (0)	22.1 (9.5)	22.1 (28.8, 15.3)
Tibamal® :						
Baseline	0.0 (0)	0.0 (0)		0.0 (0)	0.0 (0)	
Follow-up	0.0 (0)	30.7 (25.7)	30.7 (48.9, 12.6)	0.0 (0)	21.7 (9.7)	21.7 (28.5, 14.9)
Amodiaquine:						
Baseline	57.6 (17.0)	51.0 (17.3)		9.6 (6.6)	17.5 (16.7)	
Follow-up	24.8 (27.9)	8.9 (18.3)	-15.9 (7.7, -39.5)	4.4 (3.2)	2.9 (2.6)	-1.5 (1.5, -4.4)
SP:						
Baseline	19.9 (18.6)	26.0 (17.7)		3.7 (3.9)	7.0 (10.3)	
Follow-up	28.5 (20.9)	20.9 (19.8)	-7.6 (12.8, -28.0)	4.9 (5.5)	4.9 (4.6)	0.0 (5.1, -5.0)
Quinine:						
Baseline	2.2 (6.7)	2.5 (7.1)		0.0 (0)	0.0 (0)	
Follow-up	10.5 (10.7)	10.2 (12.5)	-0.2 (11.4, -11.9)	0.0 (0)	0.0 (0)	0.0 (0)
Other drugs:						
Baseline	6.7 (14.1)	4.9 (9.5)		0.3 (1.0)	0.0 (0)	
Follow-up	12.4 (17.4)	6.8 (16.6)	-5.6 (11.4, -22.6)	0.3 (0.9)	0.7 (1.3)	0.4 (1.5, -0.8)

Sales of AL in both the control and intervention arms rose in outlets with clinically related training to 14% and 28% respectively. There was no AL dispensed in outlets without clinically related training at baseline. Only 1 outlet in the control arm at follow-up reported as not having any staff with clinically related training, dispensed AL. In the intervention arm, however, 24% of outlets without clinically related training dispensed AL (Figure 6.2).

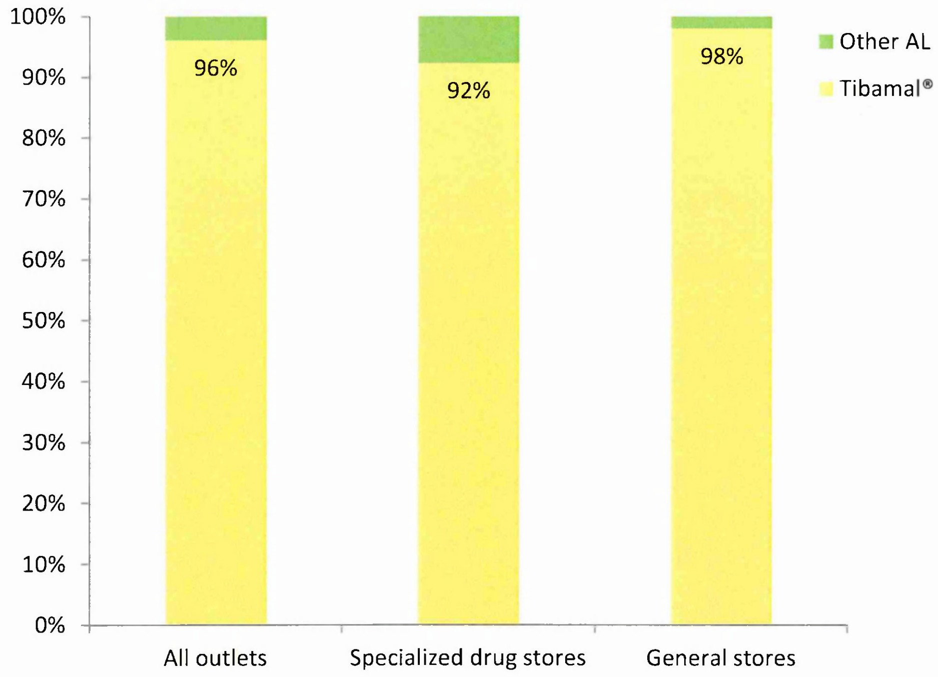
Figure 6.2: Percentage of outlets dispensing AL (including Tibamal®) to mystery shoppers, by outlet characteristic (mean of cluster summaries from the 9 intervention and 9 control clusters)



[1] Outlet types: SDS=Specialized drug stores; GS=General stores

Of outlets in the intervention arm at follow-up reported as having at least one staff with Tibamal® training, 47% dispensed AL. Of those outlets that dispensed an anti-malarial and reported having at least one staff with Tibamal® training as well as Tibamal® in stock during the provider survey 82% dispensed Tibamal® to the mystery shoppers. Tibamal® accounted for about 96% of all AL dispensed in the intervention arm at follow-up and 92% and 98% in the specialized drug stores and general stores respectively (Figure 6.3).

Figure 6.3: Tibamal® as a share of AL dispensed in the intervention arm at follow-up (mean of cluster summaries from the 9 intervention clusters)



6.2.4: Dosing of AL dispensed

The mystery shopper scenario involved a four year old child, who would be required to receive 12 tablets of AL in total, two tablets, twice daily over a period of 3 days. At baseline neither of the outlets dispensing AL (n=2) dispensed it at the correct dose. At follow-up, in the intervention arm 97.4% (75/77) of outlets dispensed the correct dose compared to 16.7% (1/6) in the control arm. At follow-up, 81.3% (26/32) of specialized drug stores dispensed the correct dose, all except one, being from the intervention arm. The percentage dispensing the correct dose was even higher in the general stores; 98.0% (50/51) dispensed the correct dose, all from the intervention arm. All the outlets that dispensed Tibamal® dosed it correctly.

6.2.5: AL counselling advice

When dispensing AL (including Tibamal®), retailers were expected to give advice to clients on how to take the AL dispensed, highlighting four key areas. First, on how to administer the drugs, they were to advise clients to give two tablets immediately and then repeat the dose after 8 hours and then twice a day for the next two days until the dose is complete. Second, on what to do if the child vomited, the retailer was expected to explain that they should repeat the dose if the child vomited within 30 minutes of taking a dose. In outlets where Tibamal® was being sold, they were to further advise the client to return to the shop and buy another dose of Tibamal® if there was need to repeat the dose, so as to replace the lost dose. Third, if the child did not get better, the client was to be advised to take the child to a health facility for further treatment. In outlets selling Tibamal®, they further needed to explain to the client the need to return to the outlet and collect a health facility referral form. Fourth, retailers needed to tell the client to give foods such as milk, bananas, honey and/or foods rich in fat.

Figure 6.4 below shows that in all the outlets that dispensed AL in the intervention arm at follow-up most gave some form of advice, mainly on how to administer drugs (over 80%) and what to do in case the child did not feel better (about 40%). However, not all outlets gave appropriate advice. The outlets did fairly poorly across all the four main advice areas, with all areas falling below 40% to as low as 3% across all outlets (Figure 6.5).

Figure 6.4: Percentage of outlets dispensing AL to mystery shoppers who provided some advice in the intervention arm at follow-up (mean of cluster summaries from the 9 intervention clusters)

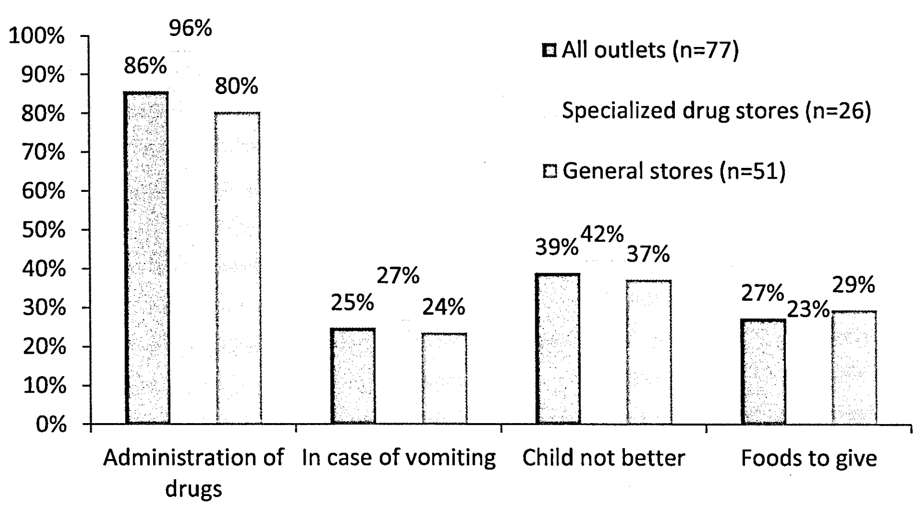
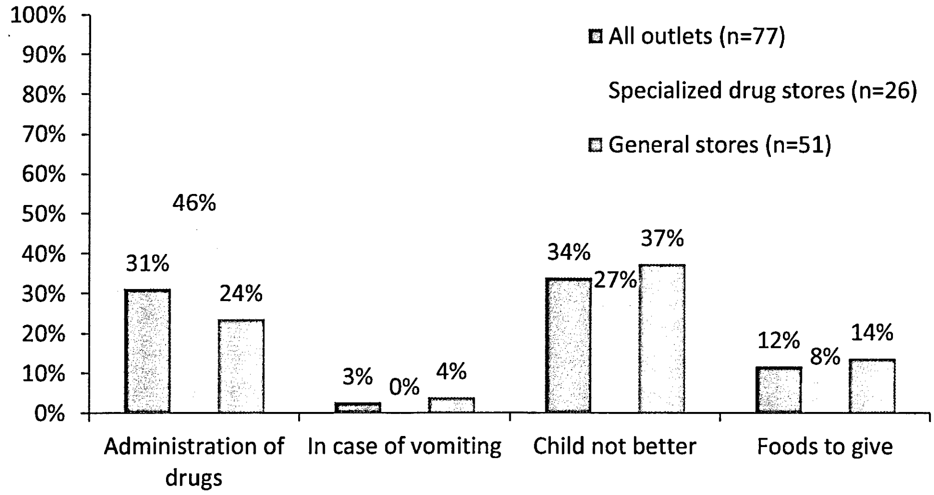


Figure 6.5: Percentage of outlets dispensing AL to mystery shoppers who provided appropriate counselling advice in the intervention arm at follow-up (mean of cluster summaries from the 9 intervention clusters)



Most appropriate advice was given on what to do if the child did not get better (34%). Specialized drug stores were more likely than general shops to give appropriate advice on how to administer the drugs (46% v. 24%) and general stores were more likely to give appropriate advice on what to do if the child did not get better (37% v. 27%). Advice on what to do if the child vomited and the appropriate foods to give was particularly poor in both specialized drug stores and general stores (Figure 6.5). None of the outlets that dispensed Tibamal® during the survey reminded the mystery shoppers to come back and buy a pack of Tibamal® in case a dose is repeated, and only 9.5% (7/74) advised them to come back for a referral form to the health facility if the child did not get better. At baseline, only 2 doses of AL were dispensed and both were from specialized drug stores in the control arm (Figure 6.2); in both cases appropriate advice was only given on what to do in case the child does not feel better. At follow-up, in the control arm there were 6 doses of AL dispensed (Figure 6.2), all of which were from specialized drug stores. As at baseline, appropriate advice was only given on what to do if the child did not get better by 3 outlets.

6.2.6: Median price charged for an AL dose

At baseline, there were only 2 doses of AL sold at a cost of 200 KSH (2.46 USD) and 180 KSH (2.22 USD). At follow-up, the 12 tab Tibamal® was sold at a median price of 20 KSH (0.25 USD, IQR: 20-20) which was the recommended retail price. Of those not paying the recommended price, two paid 30 KSH (0.37 USD), another two paid 40 KSH (0.49 USD) because of buying two packs of the 6 tab to meet the required dose, and one other paid 60 KSH (0.74 USD). Other AL sold at a median cost of 60 KSH (0.74 USD) in both arms for 6 tabs, and 80 KSH (0.98 USD) in the control arm for the 12 tab AL (Table 6.11).

Table 6.11: Median price[1] charged for an AL dose at follow-up (cluster summaries from the 9 intervention clusters)

	6 tab Tibamal® (range)	12 tab Tibamal® (range)	6 tab any other AL (range)	12 tab any other AL (range)
Intervention	- (n=0)	20 (20-60) (n=74)	60 (20-100) (n=2)	20 (20-20) (n=1)
Control	- (n=0)	- (n=0)	60 (40-150) (n=3)	80 (80-80) (n=1)

[1] Source of exchange rate: http://www.exchangerate.com/past_rates_entry.html. Accessed 13/4/2010. On 1st November 2008, when the subsidized drugs were first distributed, 1 US dollar was equivalent to 81.23 KSH.

6.3: DISCUSSION

Some limitations of the mystery shopper survey should be noted. Due to the covert nature of the survey close supervision was not feasible; it could be possible that in a few instances, the mystery shopper may have visited the wrong outlet as they relied on directions given by colleagues and deliberately did not visit outlets they had previously been to themselves during the census. In addition, given the prior consent process, it cannot be ruled out that there may have been retailers who were suspicious and therefore altered their behaviour and the advice they gave to the mystery shopper visiting their outlet. However, if this were the case then the data would display 'best practice' of providers, which still shows considerable room for improvement, especially in areas such as the provision of appropriate counselling. Finally, in our scenario, the mystery shoppers waited for the retailer to recommend treatment and paid whatever price they were asked to. However in practice, the consumer often asks for a specific treatment instead of the provider recommending it and may also bargain on the retail price, a possible limitation. Despite randomising sub locations to control and intervention arms, some outcome indicators were not equal across both arms. The reasons for the differences observed between the arms at baseline are not clear however it is known that cluster randomised controlled trials are susceptible to imbalances especially with small numbers of clusters. However, these imbalances have been controlled for in the adjusted analyses (refer to chapter 4, data analyses). For certain indicators which contained data raising the possibility of a differential effect between the arms but do not necessarily appear to be of statistical significance, a difference in difference analysis was carried out. The limitations of such an analysis have already been described in Chapter 4, however for these indicators it was thought that carrying out such an analysis may provide better insight into the data. Generally, the difference in difference outcomes gave similar significance outocmes to those originally calculated, except for reasons given for retailers not dispensing any drugs, where unlike the original analysis, 'having no anti-malarials in stock' became a significant factor and 'referring patients to a health facility' became insignificant.

The intervention improved access to AL treatment by significantly increasing AL availability as evidenced by the increased dispensing of AL in the intervention arm at follow-up to 25% of mystery shoppers as compared to 2% in the control arm. This was consistent with the 32% points difference between the arms at the provider level in the availability of AL in retail outlets as described in Chapter 5. Majority of outlets dispensing AL dispensed at the correct dose and price. The price of the only AL dose dispensed at follow-up in the control arm was 80 KSH (0.98 USD) for 12 tablets compared to a median of 20 KSH (0.25 USD) in the intervention arm, a marked difference of 60 KSH (0.74 USD). The percentage of outlets dispensing AL increased significantly in both general stores, and specialized drugs stores and all outlets of both types that dispensed Tibamal®, dosed it correctly. One of the aims of the on-going AMF-m is to crowd out anti-malarial monotherapies. These results can be cautiously interpreted to show how this could work as AL market share increased in the intervention arm, while overall antimalarial provision did not change. However, it should be noted that anti-malarial monotherapy provision also declined by 5%in the control area.

Despite this increase in sales, in the intervention arm at follow-up, AL was sold to mystery shoppers in only 25% of the outlets. Possible reasons for this have been discussed in Chapter 5 and include that even where outlets had trained staff, AL may not have been dispensed because it was not in stock; all trained shops were given the option of stocking AL but not all did so: 86% of trained outlets had antimalarials in stock during the provider survey but only 69% had AL in stock. Many not stocking AL blamed insufficient funds, with other reasons given being a change in type of business and the person trained having left the outlet. Another potential reason for lack of AL stocks could be temporary stock outs of Tibamal® due to supply problems. The provider survey showed that 32.5% of Tibamal® trained outlets reported stock outs of AL within the past 2 weeks from the day of the survey, and 9% of outlets in the intervention arm that reported usually stocking Tibamal® were out of stock on the day of the survey (Chapter 5). During one of the FGDS, one of the retailers commented that, *they only supply once a month and...You will find that they only give one...one packet and it ends..... Then in the middle of the month we are without Tibamal®'*. During the study, drugs were being supplied directly to the outlets so as to curb possible contamination between control and intervention areas. The comments raised by the retailers highlight the challenge of identifying and maintaining a steady supply of sufficient drugs in such a restricted context. Supply could likely be improved by use of established supply distribution channels.

If only those intervention outlets are considered which had a staff member who had attended Tibamal® training, and had Tibamal® in stock during the provider survey, 60% dispensed Tibamal® to the mystery shoppers. Of the 40% (39 outlets) that did not dispense Tibamal®, 16 (mainly general stores) referred the mystery shopper to a specialized drug store, 13 (mainly drug stores) dispensed another anti-malarial (mainly SP), 6 dispensed an antipyretic only, 3 referred to a general shop, and 1 referred to a health facility. The reasons for these behaviours remain unclear, but it is possible that trained staff members did not recognize the mystery shopper scenario as appropriate for Tibamal® treatment, that the staff member who received training was not present at the time of the mystery shopper survey, or that, although Tibamal® was in stock during the provider survey, it was not in stock at the time of the mystery shopper visit. The review from Rowe *et al.,* (2005) explores factors that may prevent providers from translating knowledge from training into practice. Some of these factors have been briefly described in Chapter 2. What is encouraging is that in the sub population of outlets that reported having at least one staff trained on Tibamal® and had Tibamal® in stock, 82% that dispensed an antimalarial dispensed Tibamal®.

Retailers dispensing AL were expected to ask about signs of severe disease that would determine need for referral to a facility. However, they did not routinely ask about these signs both at baseline and follow-up. Even in outlets with a Tibamal® trained employee, only 41% asked about signs of severe disease. Those outlets with an employee with clinical training did not do much better. A significant difference (6% points) was seen in direct referrals to a health facility at follow-up between intervention and control arms, with intervention outlets being less likely to refer.

Retailers were poor at giving advice to clients to whom they dispensed AL. In the intervention arm at follow-up, outlets did not accomplish the 4 advice tasks expected of them. Majority of outlets (over 80%) gave some form of advice on how to administer the drugs and

40% on what to do if the child did not feel better. The advice given though was not usually appropriate, as less than 35% of outlets gave appropriate advice on how to administer the drugs and on what to do if the child did not feel better. Advice on what to do if the child vomited and appropriate foods to give with the drugs was particularly poor, falling as low as 3%. One possible reason for this could be the poor availability of job aids in retail outlets, observed in the provider survey (Chapter 5). Job aids were deigned to help improve dispensing practices. However it should be noted that poor provision of advice is also common among health workers at health facilities. One report from Kenya showed that health workers from public, NGO and FBO facilities gave advice on what to do if the child vomited in only 7.8% of the cases of children aged less than 5 years receiving AL (DOMC, 2010). This demonstrates a generic need across providers for more innovative strategies to aid in ensuring dispensing guidelines are adhered to on a constant basis.

Summary: In summary, the mystery shopper survey showed that the intervention led to a significantly larger percentage of providers prescribing AL for the treatment of fever in a four year old child. More than 90% of providers dispensing AL dispensed the correct dose. Providers were also able to pass on the treatment subsidy to caregivers, selling Tibamal® at the recommended retail price of 20KSH. However, the intervention did not improve the percentage of providers enquiring about signs and symptoms of severe disease nor was it able to significantly increase the percentage of providers giving appropriate advice on administration of AL, and what to do if the child vomits or does not improve. The following chapter (Chapter 7) presents the household survey. This chapter reveals how findings from the provider and mystery shopper survey translated into the impact of the intervention on the proportion of children under five being treated promptly with appropriate anti-malarial treatment, within the community.

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CHAPTER 7

HOUSEHOLD SURVEY

7.1: INTRODUCTION

This chapter reports the results of the household surveys. These surveys addressed specific objective 1 of the thesis (To determine the impact on the proportion of children under five with fever being treated promptly with appropriate anti-malarial treatment, and adhering to the correct dose) and objective 3 (To determine distribution of benefits of retail sector delivery of AL by socio- economic status), and also contributed to objective 2 (To determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years).

At both baseline and follow-up, the household survey questionnaire was administered to all household heads or their representatives on household demographics and wealth. Caregivers were interviewed on any children under five years who had experienced a fever within two weeks prior to the interview. At follow-up, further information was gained from the household head on fevers experienced in members five years and above, to assess the number of non-targeted members using Tibamal® as a form of treatment.

The results are presented in section 7.2. Section 7.2.1 describes the characteristics of children sampled. Section 7.2.2 and 7.2.3 focus on those children who have had a fever within the two weeks prior to the interview, to assess the impact of the intervention on how caregivers go about treating these children's fever. This includes where they seek treatment, and the type of treatment obtained. Of those children who obtained appropriate treatment, further analysis is presented in Section 7.2.4 on the effect of the intervention on whether the dose and advice given by the provider was correct and if the caregiver was able to administer the medication in the correct manner to the child. This is followed in section 7.2.5 by analysis of whether the intervention changed caregivers' knowledge on malaria and its treatment. In Section 7.2.6 and 7.2.7 other aspects of the intervention are evaluated such as its effect on the cost of fever treatment in children and physical access to effective malaria medication. The results end by looking at how well the intervention did in limiting its exposure to the target population (Section 7.2.8). The results are discussed in Section 7.3.

7.2: RESULTS

7.2.1: Characteristics of sampled children three to 59 months

Interviews were completed at 2,319 homesteads at baseline (3,288 households), and 2,204 homesteads at follow-up (3,182 households). Data were collected on 2,749 children between three to 59 months at baseline (1,381 and 1,368 in the control and intervention arms respectively), and 2,662 at follow-up (1,305 and 1,357 respectively) (Table 7.1). In the following, all results will be addressing this age group, unless otherwise specified.

Children were evenly distributed between the districts in both arms, with around one third of sampled children residing in each district. Around half the children were male. Just under half had slept under an insecticide treated net (ITN) the night before the interview at baseline, and just over half at follow-up. Reported fever within two weeks prior to the interview ranged from 26% in the control arm at baseline to 32% in the intervention arm at follow-up. Around half the household heads for the sampled children had completed primary school or above. Sampled children were relatively equally distributed across the different wealth quintiles (Table 7.1). Fewer homesteads needed to be visited to find one childhood fever than originally estimated, resulting in more fevers being detected than expected from the sample size calculation.

The intervention was designed to improve treatment of malaria specifically in children 3 to 59 months. This age group formed roughly 95% of the under five population.

Table 7.1: Characteristics of surveyed children aged 3-59 months (mean of cluster summaries from the 9 intervention and 9 control clusters)

Characteristic	Baseline		Follow-up	
	Control % (SD[1])	Intervention % (SD)	Control % (SD)	Intervention % (SD)
Total children present in interviewed households	1,381	1,368	1,305	1,357
Percentage of children >=36 months	40.6 (3.8)	39.6 (2.1)	43.1 (4.1)	42.1 (3.3)
Male	50.5 (3.6)	53.1 (3.9)	51.6 (3.4)	52.1 (2.9)
Household heads had completed primary school or above	54.7 (8.5)	47.8 (6.9)	53.2 (9.4)	47.5 (8.4)
Slept under an ITN[1] last night	49.7 (9.2)	46.2 (5.6)	57.1 (7.7)	57.8 (10.3)
Wealth quintile[2]				
Quintile 1 (most poor)	20.6 (8.9)	21.9 (6.3)	20.1(8.6)	23.6 (7.2)
Quintile 2 (very poor)	22.7 (9.3)	21.3 (7.6)	22.3 (8.2)	23.2 (8.8)
Quintile 3 (poor)	18.0 (3.8)	21.0 (4.5)	19.0 (5.0)	20.1 (5.7)
Quintile 4 (less poor)	19.6 (6.8)	19.8 (7.2)	18.7 (10.6)	19.5 (9.7)
Quintile 5 (least poor)	19.1 (6.9)	16.0 (4.5)	19.9 (8.7)	13.3 (4.6)
Fever prevalence within the past two weeks	26.0 (8.6)	30.3 (8.7)	27.0 (7.4)	32.4 (10.3)

[1] ITN= Insecticide treated net; SD= standard deviation
[2] Wealth quintiles are based on all households interviewed. The percentages represent the number of households with children 3-59 months that fall within each quintile.

7.2.2: Treatment seeking behaviour of caregivers of children 3-59 months

Over 86% of children who experienced a fever within two weeks of the interview had some kind of action taken by the caregiver to treat the fever. There were no significant differences seen in the actions taken at follow-up across the two arms (p>0.05) (Table 7.4). Caregivers made a total of 779 actions at baseline across both arms, and 728 at follow-up (some caregivers took more than one action for a given fever). Of all actions taken, the most common were visits to government facilities and specialised drug stores (each accounting for around a third) (Table 7.2). These were followed by visits to general stores and missionary/private health facilities, with use of traditional healers very rarely reported. When the analysis was restricted to first actions only, similar patterns were observed. Analyses were carried out to see whether the intervention had affected use of retailers for fever treatment. Although there was no significant difference between the arms in the proportion of visits to the general shop or specialised drug store visits (Table 7.2), an increase was seen in the number of visits to general stores and a decrease in visits to specialised drug outlets from baseline to follow-up, in both arms.

Table 7.2: Actions taken for treating children aged 3-59 months with fever in the previous two weeks (a comparison of 9 intervention and 9 control clusters).

Care sought:	Control (N^3=9) % (SD^3) n^3	Intervention (N=9) % (SD) n	Difference in means (95% CI^3)	P-value[1] Unadjusted *Adjusted*
Government facility:				
Baseline	32.6 (12.6) 119	27.6 (14.9) 137		
Follow-up	36.4 (15.1) 118	29.0 (10.6) 116	-7.4 (5.7, -20.4)	0.2483 *0.1018*
Specialised drug store:				
Baseline	34.2 (12.9) 113	42.0 (13.1) 168		
Follow-up	23.8 (9.1) 78	30.4 (16.6) 121	6.6 (20.0, -6.8)	0.3140 *0.3642*
General store:				
Baseline	10.9 (5.2) 41	13.5 (5.2) 55		
Follow-up	20.3 (9.5) 67	27.2 (14.1) 115	6.8 (18.8, -5.1)	0.2442 *0.2158*
Missionary/Private facility:				
Baseline	7.4 (4.8) 24	8.7 (7.5) 30		
Follow-up	9.3 (5.0) 30	5.4 (8.5) 19	-3.9 (3.0, -10.9)	0.2504 *0.3208*
Traditional healers:				
Baseline	0.5 (1.5) 1	0 (0) 0		
Follow-up	0.7 (1.3) 2	0.6 (1.9) 2	0 (1.6, -1.7)	0.9794 *0.9994*
Others[2]:				
Baseline	14.4 (5.8) 51	8.3 (7.3) 40		
Follow-up	9.5 (6.3) 31	7.2 (3.9) 29	-2.3 (2.9, -7.6)	0.3625 *0.6592*

[1] P value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.

[2]Others include: prayers, treatment with western medications present at home and treatment with home made remedies

[3]n= Total number of visits, N=number of clusters, SD= standard deviation, CI= confidence interval

No obvious reasons could be identified for this observation. There appeared to be some indication that caregivers sourcing care from a government health facility tended to live physically closer to a public health facility than those who sourced care from other outlets, although these differences did not seem significant (appendix 11).

Further investigation was carried out at follow-up to see whether there was any difference between the intervention and control arms in the percentage of febrile children seeking care at specific outlet types by the children's characteristics (*appendix 6*). In general there were no significant differences in the pattern of seeking care from these sources between the intervention and control arms for the majority of sub-groups. However, in the intervention arm there was a larger proportion of febrile children in the younger age group (3 to <36 months) visiting general stores (difference in means 11.8% points; 95%CI: 2.7, 20.9) than in the control arm, and a larger proportion of febrile children in the older age group (36 to 59 months) visiting specialised drug stores (difference in means 21.5% points; 95%CI: 5.6, 37.3) than in the control arm (*appendix 6*).

Less than 10% of children who experienced a fever within two weeks of the interview were reported to have had a malaria test, with over 80% of the tests said to be positive (Table 7.3).

Table 7.3: Percentage of children three to 59 months with fever in the past two weeks who had a malaria test (mean of cluster summaries of the 9 intervention and 9 control clusters)

	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)
Obtained a blood test for malaria:			
Baseline	8.4 (5.8)	5.9 (2.8)	-2.5 (2.1, -7.1)
Follow-up	8.8 (5.4)	8.9 (5.3)	0.2 (5.6, -5.2)
Of those with a blood test, percentage with a positive result:			
Baseline	94.1 (12.2)	81.7 (22.9)	-12.4 (5.9, -30.8)
Follow-up	82.5 (24.3)	92.5 (14.9)	10.0 (31.6, -11.6)

7.2.3: Antimalarials obtained

Between the two study points, there was a significant increase in children 3-59 months receiving anti-malarial treatments in the intervention arm compared to the control arm, resulting in a 13.7% point difference (95%CI 2.5, 24.9; unadjusted p=0.0192; adjusted p=0.0074) between the arms at follow-up (Table 7.4).

The percentage of children receiving an anti-malarial monotherapy (mainly amodiaquine, SP and quinine) fell by 7.0% points in the control arm and 26.6% points in the intervention arm. At follow-up, the percentage of children receiving an anti-malarial monotherapy in the intervention arm was lower than that in the control arm, although this was only of borderline significance in the adjusted analysis (difference in means: -10.5%: 95%CI: -3.9,-16.9; unadjusted p=0.0036; adjusted p=0.0518) (Table 7.4). Of those receiving monotherapies, an average of 1% at baseline and 0.2% at follow-up received an artemisinin monotherapy. Further breakdown of monotherapies received from the different sources of care can be found in the *appendix 7*.

The percentage receiving any brand of AL (including Tibamal®) rose by 17.5% points in the control arm and 46% points in the intervention arm, resulting in a significantly greater percentage receiving AL at follow-up in the intervention arm (difference in means: 26.4%: 95%CI: 12.6, 40.2: unadjusted p=0.0009; adjusted p=0.0001) (Table 7.4; Figure 7.1). The significant increase in children receiving any brand of AL in the intervention arm was largely due to the uptake of Tibamal®, which made up 63% of all AL received in this group. No caregivers reported purchasing Tibamal® in the control arm. Of all those children who received any brand of AL, a significant proportion received it either on the same day or following day of the fever developing (Table 7.4, see *appendix 8* for results by cluster).

Table 7.4: Anti-malarial treatment obtained for children aged 3-59 months with fever in the previous two weeks (a comparison of the 9 intervention and 9 control clusters)

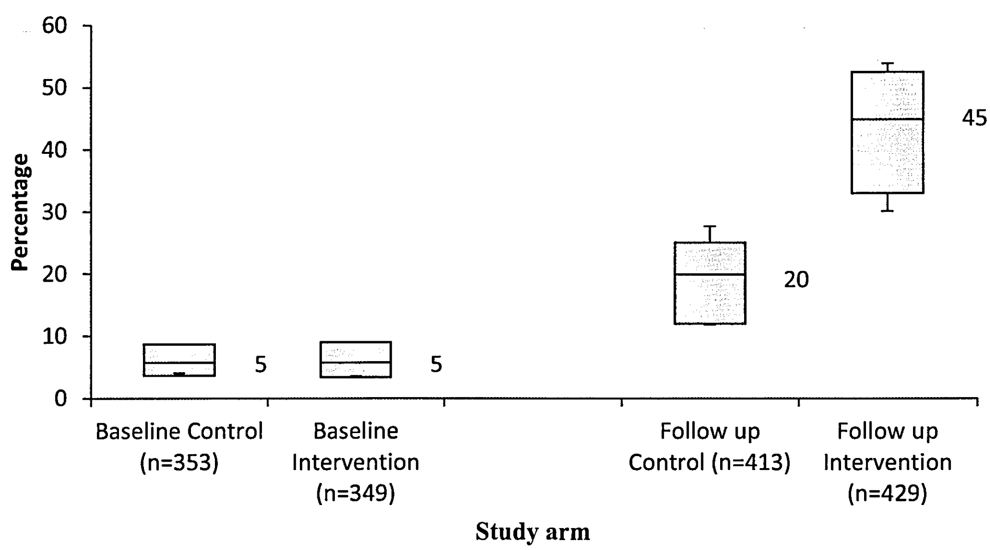
Treatment seeking behaviour indicators	Control[2] (N[7]=9) % (SD[7])	Intervention[3] (N=9) % (SD)	Difference in means (95% CI[7])	P-value[1, 9] Unadjusted *Adjusted*
Children who had care sought for them after developing fever:				
Baseline	86.6 (6.4)	90.1 (4.7)		
Follow-up	88.9 (4.3)	89.1 (4.9)	0.2(4.8, -4.4)	0.9304 *0.8759*
Children who received an antimalarial:				
Baseline	38.9 (7.8)	45.5 (9.4)		
Follow-up	50.3 (11.8)	64.0 (10.5)	13. (2.5, 24.9)	0.0192 *0.0074*
Children who received an antimalarial monotherapy:				
Baseline	29.8 (11.1)	39.0 (7.7)		
Follow-up	22.8 (7.8)	12.4 (4.8)	-10.4(-3.9, -16.9)	0.0036 *0.0518*[8]
Children who received any brand of AL:				
Baseline	9.8 (8.3)	7.7 (5.1)		
Follow-up	27.3 (15.2)	53.7 (12.3)	26.4 (12.6, 40.2)	0.0009 *0.0001*
Children who received Tibamal®:				
Baseline	0 (0)	0 (0)		
Follow-up	0 (0)	33.7 (6.8)	33.7 (28.8, 38.5)	0.0001 *0.0001*
Children who received any brand of AL on the same day or following day of fever onset:[4,6]				
Baseline	5.3 (3.2)	4.7 (3.4)		
Follow-up	19.9 (10.0)	44.9 (11.7)	25.0 (14.1, 35.9)	0.0002 *0.0001*

[1] P value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.
[2] Total number of children with fever in the previous two weeks present in the control arm: Baseline=353; Follow-up=344
[3] Total number of children with fever in the previous two weeks present in the intervention arm: Baseline=413; Follow-up=417
[4]Intraclass correlation coefficient control arm: Baseline: 0.009, Follow-up: 0.02; intervention arm: Baseline: 0.01; Follow-up: 0.01 (Based on formulae provided in Rowe A, Lama M, Onikpo F, Deming M (2002) Design effects and intraclass correlation coefficients from a health facility cluster survey in Benin. International Journal Quality Health Care 14: 521–523 [48])
[5]Test for interaction between wealth quintiles and the intervention at follow-up: For the indicator 'receiving any brand of AL on the same day or following day of fever developing', p=0.8749; for the indicator 'receiving Tibamal® on the same day or following day of fever developing', p=0.7445
[6]Rank sum test: unadjusted analysis, p=0.0013; adjusted analysis, p=0.0003
[7]SD= standard deviation, CI=confidence interval, N= number of clusters
[8]The reduced significance of the p value after adjusting mainly reflects the significant negative relationship between baseline and follow-up values for this indicator. This negative relationship is likely to be caused by a tendency for those already using some kind of antimalarial at baseline to be more likely to start using Tibamal® at follow-up (substituting one similarly priced product for another), as compared to those not using any antimalarial at baseline (for whom using Tibamal® would represent an increase in average expenditure compared with their baseline purchases).
[9]Difference in difference analysis gave similar unadjusted p values to those reported in the above indicators apart from '*children who received an antimalarial*', p value=0.1740 (*appendix 12*)

In the analysis, the proportion receiving AL on the same day of fever developing or following day in the intervention arm compared to the control remained significant at p=0.0002 (difference in means 25.0%: 95%CI: 14.1, 35.9; adjusted p=0.0001) (Table 7.4). This represents a substantial increase for this primary outcome, with the percentage of children receiving prompt AL treatment in the intervention arm being more than double that in the control arm at follow-up. There seemed to be no correlation between increasing wealth and the probability of receiving any brand of AL (p=0.8749) or Tibamal® (p=0.7445) on the same day or following day of fever developing (Table 7.4, refer to footnotes).

The variance observed between clusters was not large enough to warrant a weighted analysis (*appendix 8*) (Hayes & Moulton, 2009). Only 5.5% of homesteads had more than one child with fever in the past 2 weeks; allowing for homestead level clustering in the logistic regression did not affect the adjusted estimated.

Figure 7.1: Children 3-59 months who received any brand of AL on the same day or following day of fever developing (mean of cluster summaries of the 9 intervention and 9 control clusters)



n= total number of children with fever
Horizontal line within each box represents mean (percentage mean typed adjacent to each horizontal line), horizontal line at the top and bottom of each box represents 25% and 75% inter quartile range, error bars represent upper and lower 95% confidence intervals.

Investigations were carried out to see whether these significant differences between the intervention and control groups held for specific sub-groups defined by the child's characteristics. Significant differences were found in the probability of obtaining both any AL and Tibamal® specifically for all sub-groups investigated (Tables 7.5 and 7.6).

Table 7.5: Percentage of febrile children aged 3-59 months at follow-up who obtained any brand of AL on the same day or following day of fever onset, by child's characteristics (mean of cluster summaries of the 9 intervention and 9 control clusters).

Children obtaining any brand of AL on the same day or following day of fever onset at follow-up:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95% CI)
Total number of febrile children	344	417	
Age:			
< 36 months	21.3 (11.9)	43.3 (13.7)	22.0 (9.2, 34.8)
36-59 months	18.2 (15.2)	48.1 (12.4)	29.9 (16.0, 43.7)
Sex:			
Male	20.7 (11.5)	47.7 (9.2)	27.1 (16.7, 37.4)
Female	18.8 (10.9)	42.1 (16.8)	23.3 (9.2, 37.5)
Caregiver's education:			
Primary incomplete	15.7 (8.3)	42.6 (10.6)	26.8 (17.3, 36.3)
Primary complete and above	26.3 (14.7)	50.4 (19.1)	24.1 (7.1, 41.2)
Household head's education:			
Primary incomplete	19.6 (11.0)	46.3 (8.2)	26.8 (17.1, 36.4)
Primary complete and above	21.3 (15.2)	44.5 (17.5)	23.2 (6.8, 39.6)
ITN use:			
ITN use last night	22.1 (15.4)	48.3 (13.4)	26.2 (11.8, 40.6)
No ITN use last night	14.9 (7.1)	42.3 (16.6)	27.4 (14.7, 40.2)
Wealth quintile[5]:			
Quintile 1 (most poor)	14.8 (20.6)	38.9 (18.3)	24.1 (4.6, 43.6)
Quintile 2 (very poor)	16.6 (16.9)	40.0 (22.1)	23.4 (3.7, 43.0)
Quintile 3 (poor)	16.6 (18.6)	50.8 (33.3)	34.2 (7.3, 61.2)
Quintile 4 (less poor)	21.7 (18.6)	43.8 (22.4)	22.1 (1.5, 42.7)
Quintile 5 (least poor)	15.4 (15.9)	47.8 (24.3)	32.4 (11.9, 52.9)

[5]Test for interaction between wealth quintiles and the intervention at follow-up: For the indicator 'receiving any brand of AL on the same day or following day of fever developing', p=0.8749

Significant differences were observed between the arms for both age groups, both genders, and both ITN users and non-users. Importantly, significant differences were also found regardless of the caregiver or household head education, and for all wealth quintiles, demonstrating that all population groups appeared to have benefited from the intervention. It was notable that the percentage obtaining Tibamal® in the intervention arm at follow-up was similar across all wealth quintiles (ranging from 20.8% (SD: 22.1) in the 5th quintile to 30.4% (SD: 21.3) in the 3rd quintile).

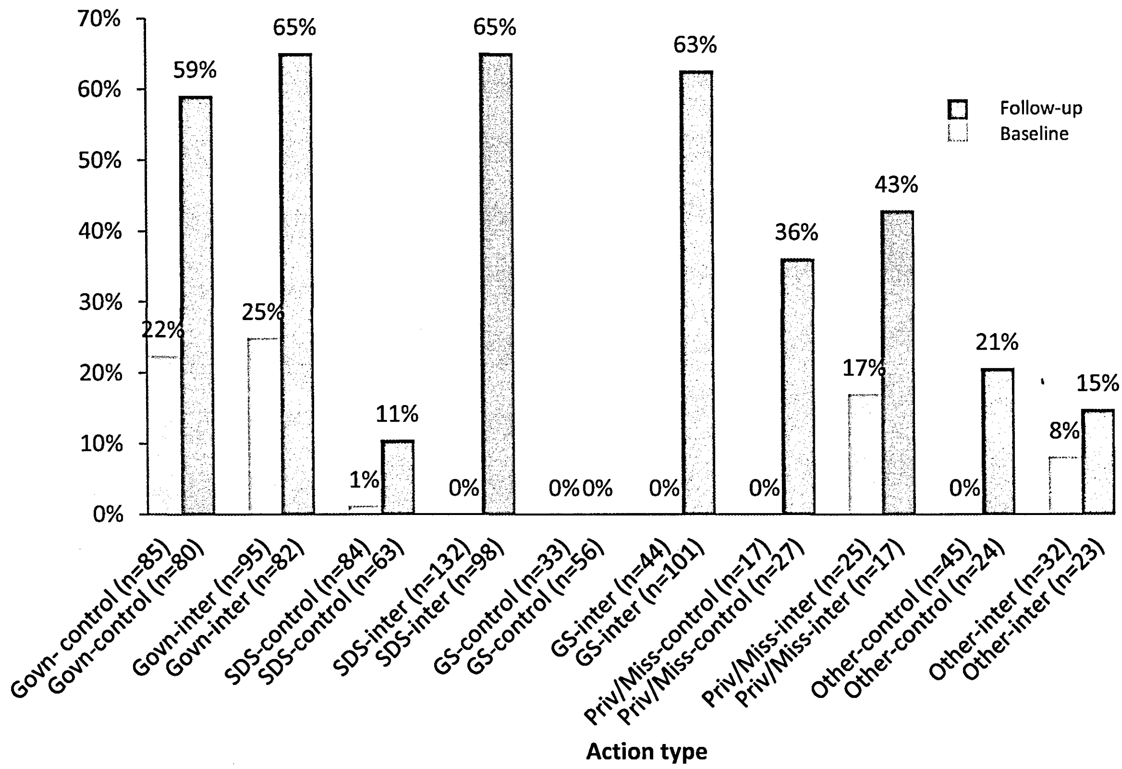
Table 7.6: Percentage of febrile children aged 3-59 months at follow-up who obtained Tibamal® on the same day or following day of fever onset, by child's characteristics (mean of cluster summaries of the 9 intervention and 9 control clusters)

Children obtaining Tibamal® on the same day or following day of fever onset at follow-up:	Control[2] (N=9) % (SD)	Intervention[3] (N=9) % (SD)	Difference in means (95% CI)
Total number of febrile children	344	417	
Age:			
3 months to < 36 months	0 (0)	27.7 (10.2)	27.7 (20.5, 34.9)
36-59 months	0 (0)	33.9 (9.2)	33.9 (27.4, 40.4)
Sex:			
Male	0 (0)	31.2 (8.5)	31.2 (25.2, 37.2)
Female	0 (0)	28.1 (16.4)	28.1 (16.5, 39.8)
Caregiver's education:			
Primary incomplete	0 (0)	26.9 (7.1)	26.9 (21.9, 31.9)
Primary complete and above	0 (0)	37.0 (17.9)	37.0 (24.3, 49.6)
Household head's education:			
Primary incomplete	0 (0)	31.9 (10.2)	31.9 (24.7, 39.1)
Primary complete and above	0 (0)	28.0 (10.8)	28.0 (20.3, 35.6)
ITN use:			
ITN use last night	0 (0)	31.2 (15.0)	31.2 (20.7, 41.8)
No ITN last night	0 (0)	26.5 (6.1)	26.5 (22.2, 30.8)
Wealth quintile[5]:			
Quintile 1 (most poor)	0 (0)	30.1 (14.3)	30.1 (40.2, 20.0)
Quintile 2 (very poor)	0 (0)	25.5 (19.9)	25.5 (39.6, 11.4)
Quintile 3 (poor)	0 (0)	30.4 (21.3)	30.4 (45.4, 15.3)
Quintile 4 (less poor)	0 (0)	32.5 (22.3)	32.5 (48.3, 16.8)
Quintile 5 (least poor)	0 (0)	20.8 (22.1)	20.8 (36.4, 5.2)

[5]Test for interaction between wealth quintiles and the intervention at follow-up: For the indicator 'receiving Tibamal® on the same day or following day of fever developing', p=0.7445

Investigations were carried out on the percentage of actions by source which resulted in any brand of AL being obtained on the same day or following day of fever developing (Figure 7.2). The significance of difference between the arms at follow-up was not assessed since the study was not powered for this type of sub-analysis. At follow-up, AL dispensing increased from zero to 65% in the intervention arm in specialised drug stores and from zero to 63% in general stores. Substantial increases were also seen at government facilities and private/ mission facilities, but similar increases were observed in both arms.

Figure 7.2: Percentage of visits to different source of care at which any brand of AL was dispensed on the same day or following day of fever developing (mean of cluster summaries of the 9 intervention and 9 control clusters)



Notes: n= total number of visits on the same day or following day of child's fever developing; Govn= government; inter= intervention; SDS= specialised drug store; GS= general store; Priv/ Miss= Private/ Missionary facility. Other includes treatment at home with home-made remedies or western medication, traditional healers or prayers.

Standard deviations for each facility: Baseline control arm: government=20; SDS=4; GS=0; priv/miss=0; other=0. Baseline intervention arm: government=32; SDS=0; GS=0; priv/miss=33; other=10; Follow-up control arm: government=18; SDS=20; GS=0; priv/miss=49; other=36; Follow-up intervention arm: government=18; SDS:21; GS=25; priv/miss=53; other=34.

7.2.4: Adequacy of AL doses obtained and consumed

Caregivers were asked to state the number of AL tablets (including Tibamal®) they were provided with and the number their child consumed, in order to assess providers' dispensing practices and children's adherence to the treatment. The accuracy of dose obtained was defined as obtaining at least the correct number of tablets for their child's age. The accuracy of dose consumed was defined as reporting consumption of exactly the correct number of tablets for the child's age within three days of receiving the medication. The precise timing of tablet consumption was not assessed due to the challenges of obtaining accurate recall for these data.

Of all children receiving any brand of AL, just under 70% in both arms obtained an accurate dose at baseline (control 69.9% (SD: 33.8); intervention 68.6% (SD: 35.9)), and just over 70% at follow-up (control 71.6% (SD: 20.9); intervention 76.9% (SD: 7.2). Not surprisingly, no significant difference was recorded at follow-up between the two arms (difference in means 5.3%: 95% CI 20.9, -10.3; unadjusted p=0.4836; adjusted p=0.6545). Of all children obtaining AL, at baseline a correct dose was consumed by 40.5% (SD: 23.3) in the control group and 53.1% (SD: 40.2) in the intervention group. At follow-up this rose to 49.4% (SD: 24.8) in the control arm and 67.0% (SD: 8.5) in the intervention arm, but the difference was not significant at the 5% level (unadjusted p=0.0606; adjusted p=0.1095) (Table 7.7). In the intervention arm, 80.6% (SD: 9.6) of caregivers received the correct dose of Tibamal® for their child at follow-up compared to 70.7% (SD: 17.8) receiving the correct dose of any other brand of AL. Adherence to Tibamal® was 71.8% (SD: 11.8) compared to adherence to any other brand of AL at 61.1% (SD: 22.5) also at follow-up in the intervention arm.

Table 7.7: Adequacy of AL doses obtained and consumed (mean of cluster summaries from 9 intervention and 9 control clusters)

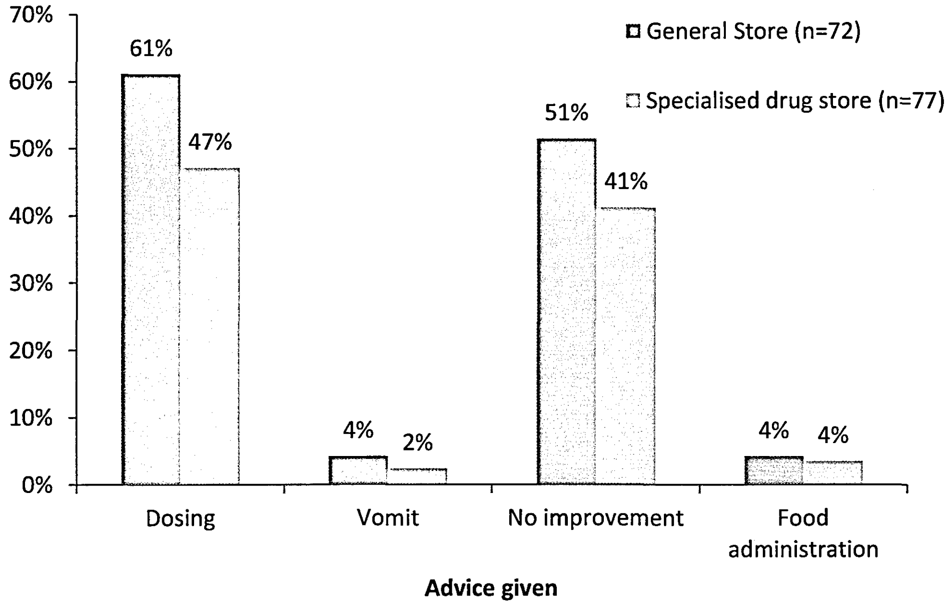
	Control[2] (N[4]=9) % (SD[4])	Intervention[3] (N=9) % (SD)	Difference in means (95% CI[4])	P-value[1] Unadjusted *Adjusted*
Adequacy of dose obtained from the provider:				
Baseline	69.9 (33.8)[5]	68.6 (35.9)		
Follow-up	71.6 (20.9)	76.9 (7.2)	5.3 (20.9, -10.3)	0.4836 *0.6545*
Adequacy of dose administered:				
Baseline	40.5 (23.3)[5]	53.1 (40.2)		
Follow-up	49.4 (24.8)	67.0 (8.5)	17.6 (36.1, -0.9)	0.0606 *0.1095*

[1] P value: The p value appearing on top refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. The p value underneath in italics refers to the level of significance of the adjusted difference between the control and intervention arm at follow-up.
[2] Total number of doses in the control arm: Baseline=26; Follow-up=89
[3] Total number of doses in the intervention arm: Baseline=30; Follow-up=221
[4] N= number of clusters, SD= standard deviation, CI= confidence interval
[5] cluster summary from 8 clusters

Reported advice given to caregivers receiving AL thorough the retail sector was evaluated, the denominator being the total number of cases in which any kind of AL was dispensed in general stores and specialised drug stores (reported advice at facility visits was not recorded as the focus was on advice provided by outlet types targeted for training during the intervention). As only eight AL doses were dispensed from the retail sector in the control arm at follow-up, and only four doses from both arms at baseline, the analysis focuses on the intervention arm at follow-up (Figure 7.3).

The most common correct advice given in the general store was on 'how to administer the medication', given in 61.1% (SD: 24.2) of cases, compared to 47.1% (SD: 15.8) in specialised drug stores. For this indicator, advice was deemed to be correct if the caregiver was told to give their child one tablet twice daily for three days if the child was less than three years, and two tablets, twice daily for three days if the child was 3-<5years of age. Giving the first two doses 8 hours apart was not assessed. Advice on what to do if the child did not improve was given in 43% of cases in both types of retail outlet. Advice was very rarely given on actions to take if the child vomited (2.4% (SD: 5.1) in general stores; 1.2% (SD: 3.5) in specialised drug stores), or on how to give foods with the drugs (4.2% (SD: 9.6) in general stores; 2.2% (SD: 4.6) in specialised drug stores).

Figure 7.3: AL treatment advice given by source, in the intervention arm, at follow-up (mean of cluster summaries of the 9 intervention clusters)



n= total number of cases in which AL was dispensed from the sector

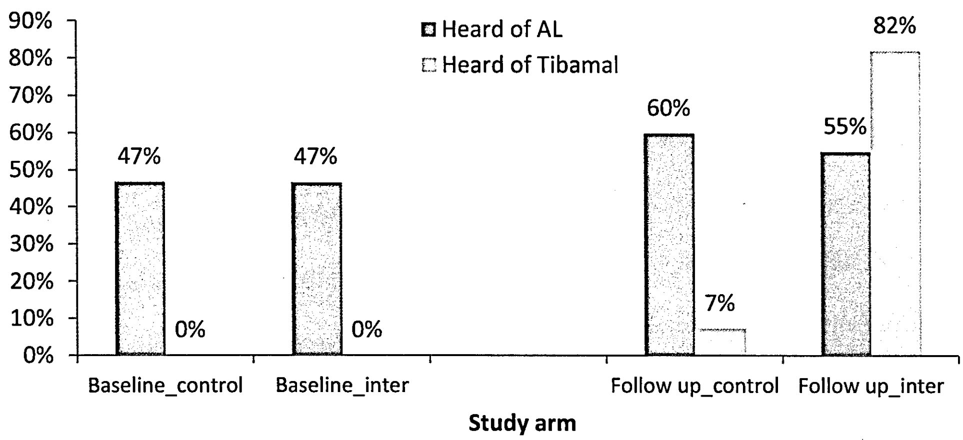
7.2.5: Caregivers' Knowledge

Data on 679 and 672 caregivers were assessed at baseline and follow-up respectively. Caregivers included in this analysis had to have had a child suffering from fever within two weeks of the interview. In this group, just over one third of all caregivers interviewed reported to have been schooled to the end of primary level and above.

Caregivers' knowledge was based on their awareness of Tibamal® and/ or AL, together with awareness on the signs and symptoms of uncomplicated and complicated malaria. Just under half of caregivers had heard of AL at baseline (Figure 7.4). This increased to 60% (SD: 20.6) in the control arm and 55% (SD: 13.3) in the intervention arm at follow-up, with no significant difference observed between the arms (p=0.5803). At follow-up 82% (SD: 9.5) in the intervention arm had heard of Tibamal®, which was 74.5% points greater (95%CI: 66.4, 83.2, p=0.0001) than those that had heard of Tibamal® in the control arm. 40% of the 26 caregivers in the control arm reported having heard of Tibamal® from healthcare staff (Figure 7.5). In the intervention arm 16% had heard of Tibamal® from healthcare staff, a similar percentage (17%) from other people (friends, family and colleagues), and 12% from the PSI wall paintings and '*barazas*' (Figure 7.6).

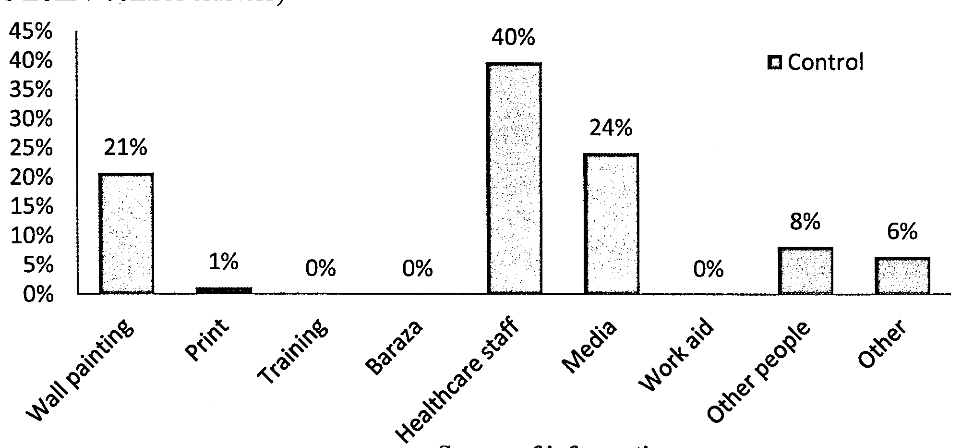
In both arms, some caregivers reported having heard of Tibamal® from the radio (media). Tibamal® was not advertised on the radio, but one of the members from the DHMT in Butere-Mumias reported having heard an interview on the radio with a youth group where Tibamal® was mentioned as a cure for malaria that could be accessed in the communities (communication with District Medical Officer for Butere).

Figure 7.4: Knowledge of Tibamal® and AL (mean of cluster summaries of the 9 intervention and 9 control clusters



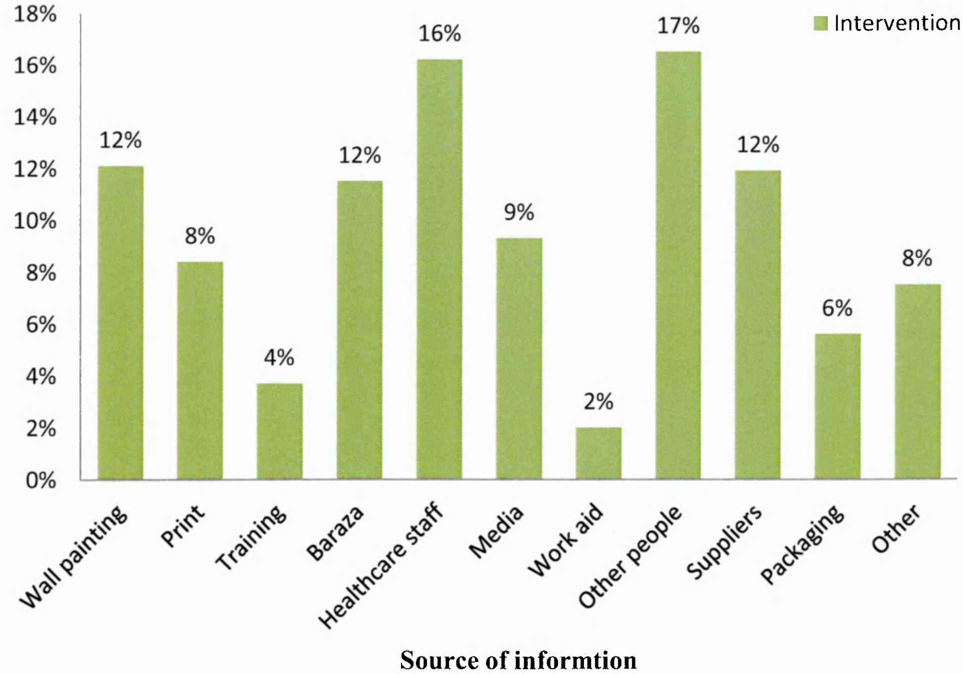
inter=intervention; Number of caregivers (denominator): Control arm: baseline=316; follow-up=276, Intervention arm: baseline= 363; follow-up=326

Figure 7.5: Source of Tibamal® information at follow-up in the control arm (mean of cluster summaries from 7 control clusters)



n (number of caregivers who have heard of Tibamal®)=26
Other = seeing the packaging, Tibamal® promotional t-shirts.

Figure 7.6: Source of Tibamal® information at follow-up in the intervention arm (mean of cluster summaries from 9 intervention clusters)



n (number of caregivers who have heard of Tibamal®)=321
Other includes Tibamal® promotional t-shirts and shopkeepers selling the medication.

Caregivers were asked to mention symptoms they would expect to see in a child of four years suffering from uncomplicated malaria. Of all reported symptoms, fever was most commonly mentioned (average of 69% and 83% between the arms, at baseline and follow-up respectively), followed by vomiting (average of 32% and 40% between the arms, at baseline and follow-up respectively) (Figures 7.7 and 7.8). The knowledge of uncomplicated malaria symptoms remained similar between arms at the two time points. There was a 10% point increase in the reporting of fever as a common symptom from baseline to follow-up, however this increase was seen in both arms. For complicated malaria, caregivers were most knowledgeable of children of four years being unable to eat (average of 30% and 43% between the arms, at baseline and follow-up respectively). The knowledge of complicated malaria symptoms also remained similar between the arms at follow-up. In general, symptoms of uncomplicated malaria were better known than complicated malaria (Figure 7.9 and 7.10).

Figure 7.7: Caregivers' knowledge of symptoms of uncomplicated malaria in a four year old, baseline (mean of cluster summaries of the 9 intervention and 9 control clusters)

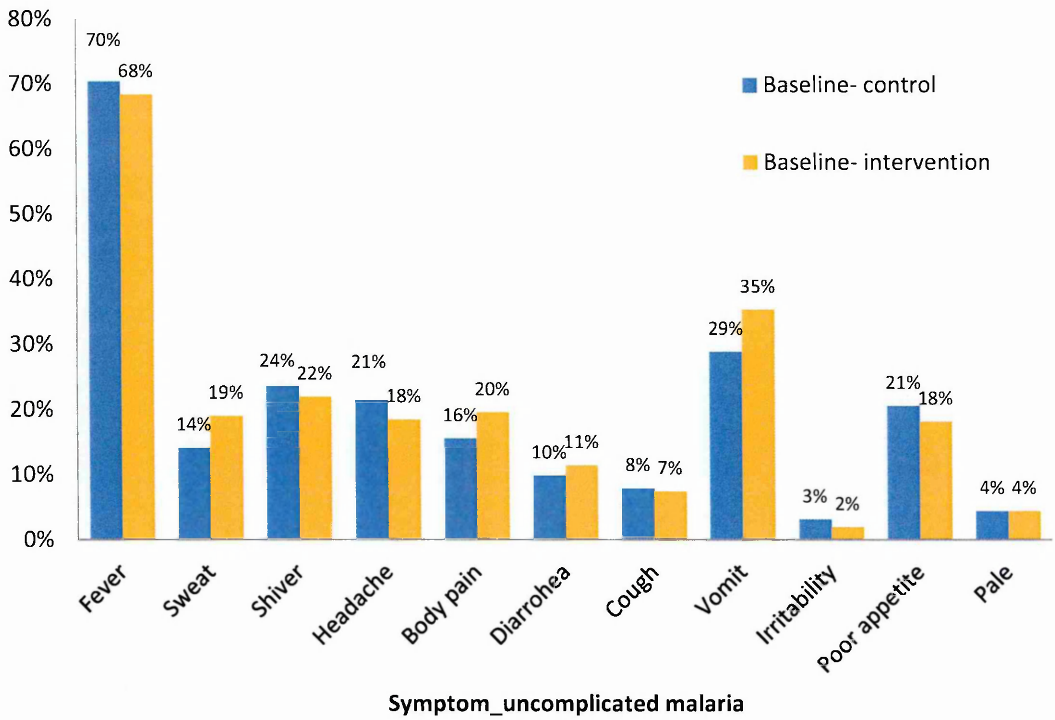


Figure 7.8: Caregivers' knowledge of symptoms of uncomplicated malaria in a four year old, follow-up (mean of cluster summaries of the 9 intervention and 9 control clusters)

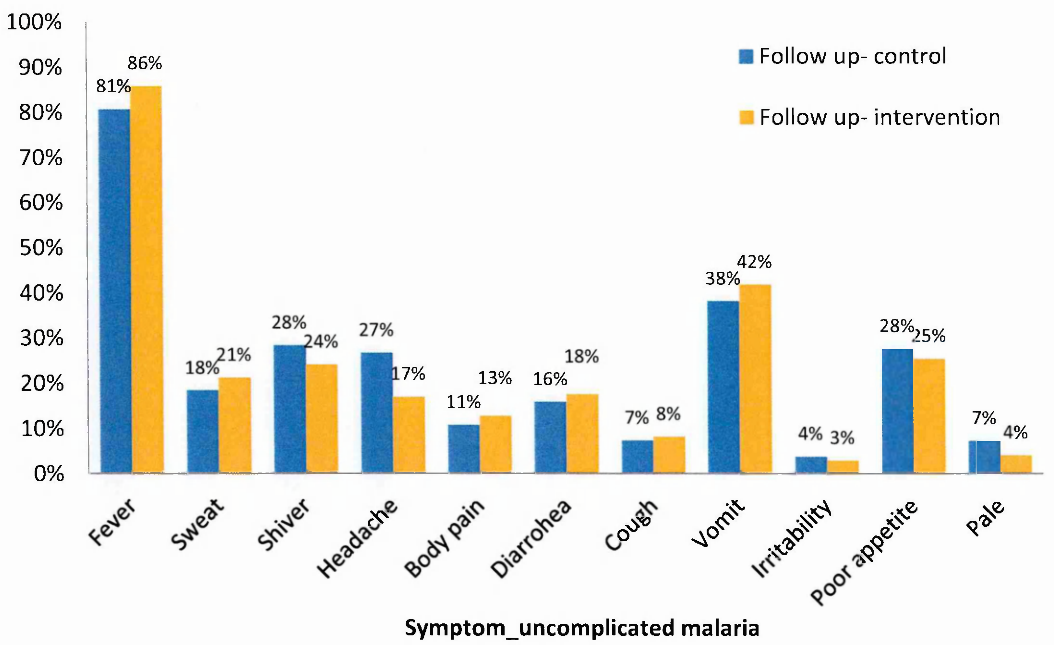


Figure 7.9: Caregivers' knowledge of symptoms of complicated malaria in a four year old, baseline (mean of cluster summaries of the 9 intervention and 9 control clusters)

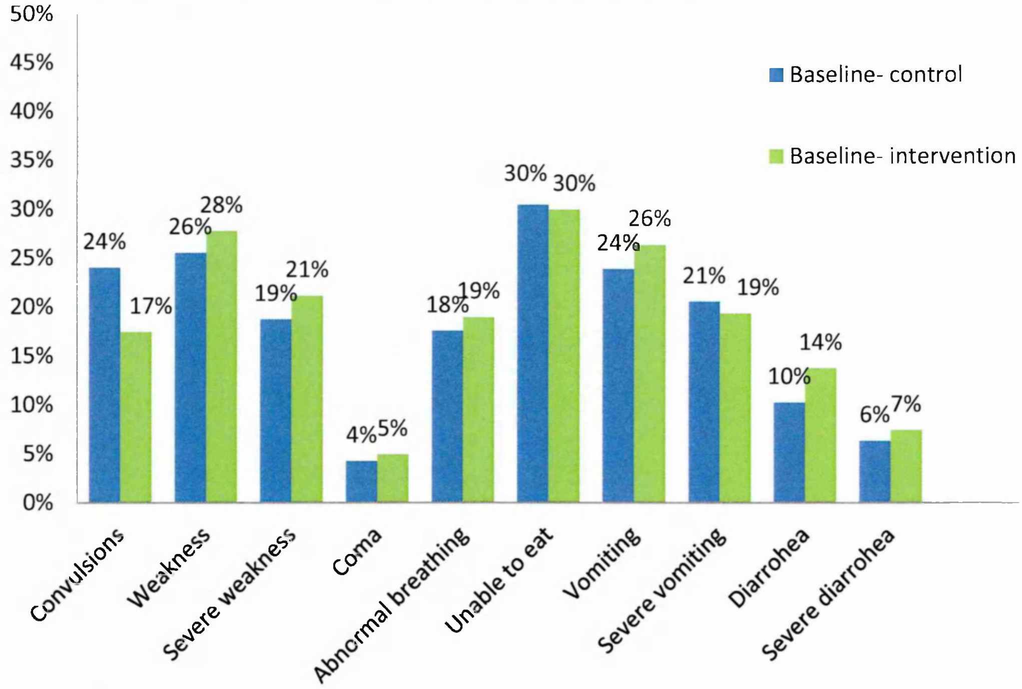
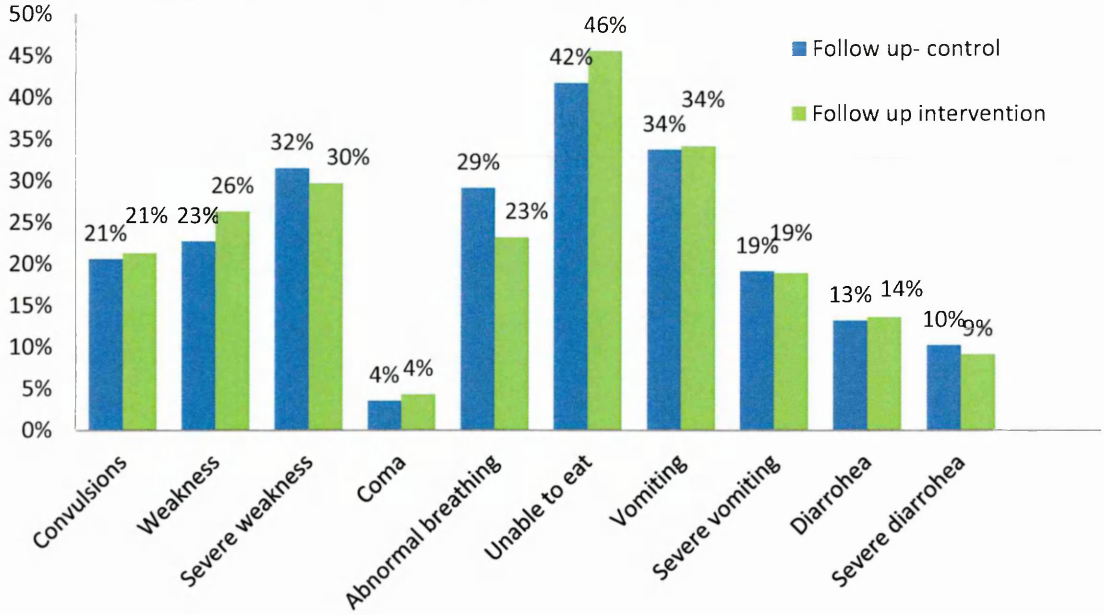


Figure 7.10: Caregivers' knowledge of symptoms of complicated malaria in a four year old, follow-up (mean of cluster summaries of the 9 intervention and 9 control clusters)

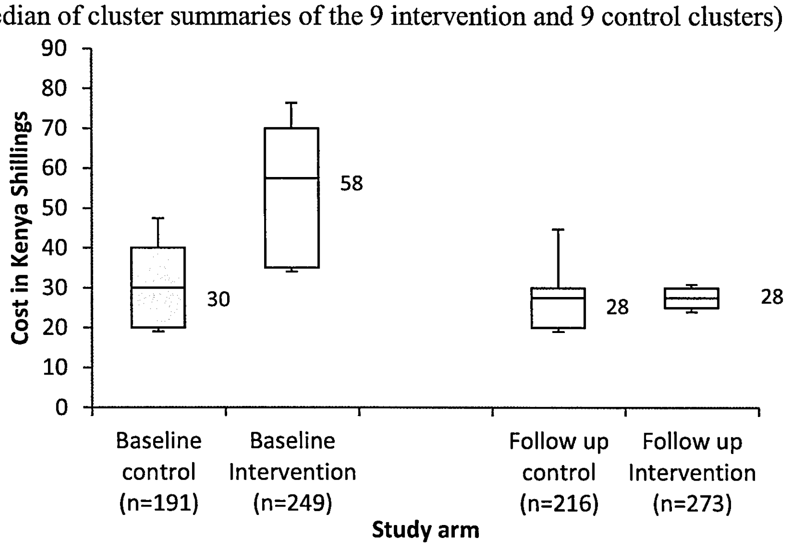


7.2.6: Household cost of fever treatment

Price paid for subsidised Tibamal®: 95.2% (SD: 5.87) of caregivers in the intervention arm who purchased Tibamal® at follow-up said they bought Tibamal® at the recommended retail price of 20 KSH (0.25 USD). Of those not paying this price, three paid less than 20 KSH (0.25 USD) and five paid between 25 KSH (0.31 USD) and 100KSH (1.23 USD).

Household cost of treatment seeking: The household cost of treatment seeking was defined as the total amount spent per child on travelling to and from sources of care, medications, consultation fees, laboratory tests and any other costs incurred as a direct result of seeking treatment for this illness, for example bed costs if the child was admitted. Household costs were evaluated only if the child's fever had resolved at the time of the interview (including unresolved fevers leads to under-estimation of total household costs per episode as further care may be sought after the interview). It was observed that median household spending per child's fever was higher in both arms at baseline compared to follow-up. Costs fell from 30KSH (0.37USD) to 28KSH (0.34USD) and 58KSH (0.71USD) to 28KSH (0.34USD), in control and intervention arms respectively (Figure 7.11), with no significant difference between the arms at follow-up (unadjusted p= 0.6143; adjusted p=0.1925).

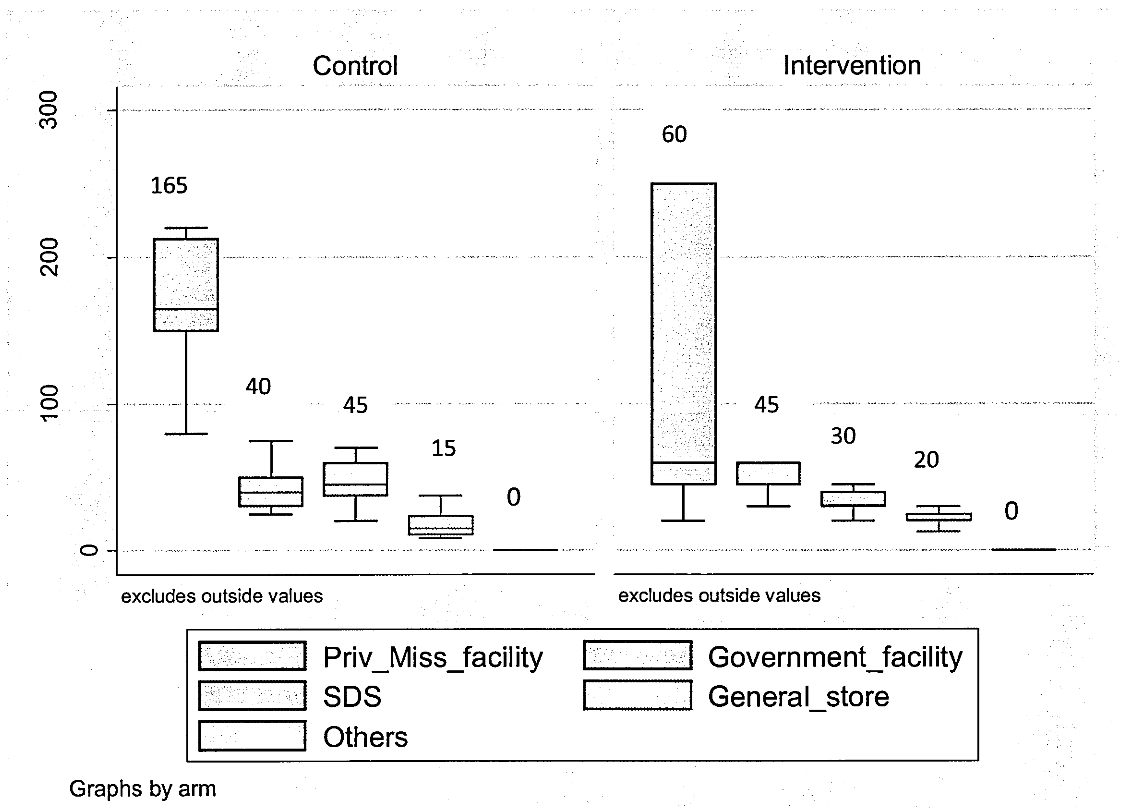
Figure 7.11: Household cost of treatment seeking per completed episode of childhood fever (median of cluster summaries of the 9 intervention and 9 control clusters)



n= total number of children with resolved fevers
Horizontal line within each box represents median spending, horizontal line at the top and bottom of each box represents 25% and 75% inter quartile range, error bars represent upper and lower 95% confidence intervals, numbers adjacent to each box represent median KSH.

The median costs incurred per provider visit showed that caregiver spending was highest for visits to private/ mission health facilities (averaging 113 KSH (1.39 USD) across the arms), followed by specialised drug shops and government facilities (both averaging at around 40KSH (0.49USD) across the arms), with the lowest costs incurred for care from general stores (averaging 18 KSH (0.22 USD) across the arms) (Figure 7.12). Costs incurred from prayers, visiting a traditional healer or treatment with either home made remedies or western medications found at home were negligible.

Figure 7.12: Household cost per provider visit at follow-up (median of cluster summaries of the 9 intervention and 9 control clusters)



.n (total number of visits to outlet): Control arm- Priv_miss_facility=30; Government_facility=118; SDS=76; General_store=67; Others=33. Intervention arm- Priv_miss_facility=19; Government_facility=115; SDS=121; General_store=115; Others=28

.Horizontal line within each box represents median spending, and numbers above each box quantifies median spending in Kenya shillings. Horizontal line at the top and bottom of each box represents 25% and 75% inter quartile range, error bars represent upper and lower 95% confidence intervals. .Priv_Miss_facility= private/ missionary health facilities; SDS= specialised drug stores. Others include treatment with western medications at home, treatment with home-made remedies and visits to a traditional healer.

7.2.7: Travel time to the nearest AL retail outlet

The average travel time at baseline was 39 minutes (SD: 13.5) in the control arm and 32 minutes (SD: 15.8) in the intervention arm. At follow-up travel time was significantly lower in the intervention arm, at 9.8 minutes (SD: 3.14) compared to 28.3 (13.3) in the control arm, with a mean difference of 19 minutes (95% CI: -8.8, -28.3 p= 0.0010) between the arms (Table 7.8). Further analysis of travel times at follow-up showed 91% of households in the intervention arm were less than 20 minutes away from the nearest AL outlet, while in the control this was slightly more than one third (Figure 7.15).

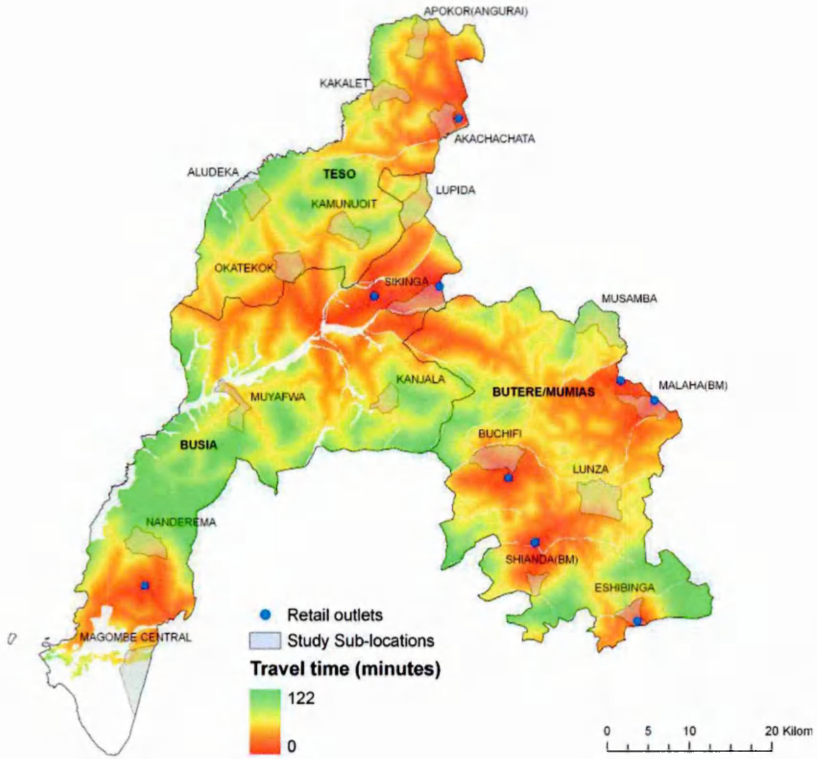


Figure 7.13: Map showing travel time in minutes to nearest retail outlet selling AL at baseline. Areas with less travel times are shaded as red in the map while those in green have greater travel times (maximum of 121 minutes). The blue dots represent the geo-located retail outlets at baseline (n= 10).

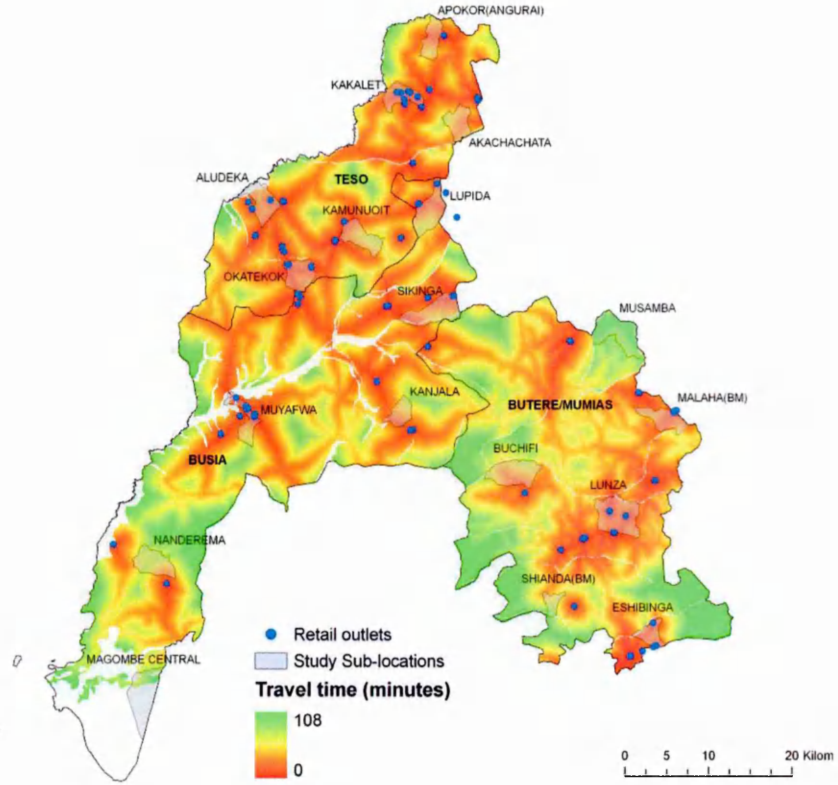


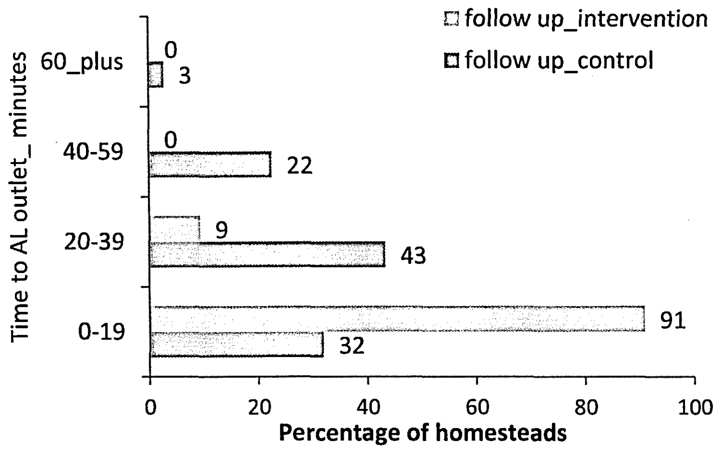
Figure 7.14: Map showing travel time in minutes to nearest retail outlet selling AL at follow-up. Areas with less travel times are shaded as red in the map while those in green have greater travel times (maximum of 108 minutes). The blue dots represent the geo-located retail outlets at follow-up (n= 165).

Table 7.8: Average travel time of homesteads to nearest retail outlet AL source in minutes (mean of cluster summaries from the 9 intervention and 9 control clusters)

Travel time to nearest AL retail outlet:	Control (N=9) % (SD)	Intervention(N=9) % (SD)	Difference in means (95% CI)	P-value[1]
Baseline	38.8 (13.5)	32.3 (15.8)	-6.5 (8.8, -21.8)	
Follow-up	28.3 (13.3)	9.8 (3.14)	-18.5 (-8.8, -28.3)	0.0010

[1]P value refers to the level of significance of the unadjusted difference between control and intervention arms at Follow-up

Figure 7.15: Average travel time of homesteads to nearest AL retail outlet at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)



7.2.8: Use of Tibamal® by non-Targeted Age Groups

Tibamal® was supposed to be used by children aged 3 – 59 months only. I therefore assessed whether the drug was used by any patients outside this age range. Tibamal® was reportedly obtained in only 0.1% of fevers in those 5 years and above in the control arm and 6.7% in the intervention arm. The median age of those 5 years and above receiving Tibamal® was 8 years. There were ten children at follow-up less than three months old who suffered a fever within two weeks prior to the survey. None of these children received Tibamal®, though two did receive AL from government health facilities (Table 7.9).

Table 7.9: Use of Tibamal® in non-targeted household members reporting fever, at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

Household members aged:	Control (N=9) % (SD)	Intervention (N=9) % (SD)
5 years and above	0.1 (25.9)	6.7 (3.8)
Less than three months	0 (0)	0 (0)

Total number of people five years and above with fever in the past two weeks, in the control arm=1,003; intervention arm=1,049

7.3: DISCUSSION

There has been considerable debate about how access to and quality of malaria treatment can be improved (Arrow *et al.,* 2004; Goodman *et al.,* 2007; Smith *et al.,* 2009; D'Alessandro *et al.,* 2005; Oxfam 2009). This chapter shows that a suite of ACT subsidies, retailer training, and community awareness activities can lead to substantial improvement in the uptake of prompt effective treatment for febrile children in rural Kenya. Although coverage still fell well below the 80% target set by the RBM, the percentage of children receiving AL during a fever episode in the intervention arm was more than double that in the control arm at follow-up, with more than half of those receiving Tibamal®, usually on the same day or the following day after fever onset. This was accompanied by a significant fall in the proportion of children being treated with antimalarial monotherapies. This is likely to have reflected "crowding out" of these antimalarials by the more effective subsidised AL. It may also have reflected government directives to phase out monotherapies such as amodiaquine at this time (personal communication with PPB and local amodiaquine manufacturer), though this would have affected both the control and intervention arms. In the vast majority of cases, subsidised AL was purchased at the recommended retail price. The intervention was able to bring AL physically closer to the community.

The increase in AL coverage observed does not appear to have resulted from a change in choice of providers, with treatment seeking patterns remaining relatively constant before and after implementation in both arms. Instead, the intervention appears to have led to a change in the type of drugs dispensed in specialised drug and general retail outlets, with a major shift towards AL in both of these provider types.

It was notable that a substantial increase was also seen in AL coverage in the control arm between baseline and follow-up. This is likely to have reflected a reduction in AL stock outs at government facilities between the two surveys in both arms. At baseline public sector AL stock outs were common, with only one third of facilities serving the study areas stocking both the six and twelve tablet packs of AL (Kangwana *et al.,* 2009), whereas at follow-up stocks had almost doubled to 65% (*appendix 9*). This highlights that ensuring health facility AL stocks is also essential for improving AL access.

The intervention was able to significantly impact on caregiver knowledge regarding Tibamal® in the intervention area, with a very high percentage having heard of Tibamal® (82%) at follow-up, exceeding the percentage that knew the name 'AL'. However, caregivers' knowledge on symptoms on uncomplicated and complicated malaria in children remained constant between the two time points.

There was no significant difference in the overall cost of care incurred by caregivers between the intervention and control areas. This was not surprising since the subsidy allowed for Tibamal® to be sold at similar prices to other antimalarial monotherapies, so a substitution from previously more popular monotherapies to Tibamal® would not be expected to change costs.

Investigations were carried out on adherence to AL in terms of both obtaining and consuming the correct dose. In the intervention arm at follow-up, 77% of children receiving AL obtained an accurate dose, and 67% consumed the correct dose. No significant difference was observed in the accuracy of doses obtained or consumed between Tibamal® (obtained only from retail outlets) and other AL brands (obtained mainly from government and private/mission facilities), although there was room for improvement in patient adherence to AL from both sources. Adherence levels fall within the varying ACT adherence levels quoted in other studies and mentioned in Chapter 2, of 39% to 90%, though the higher figures obtained in some studies may reflect study designs where caretakers were aware that their compliance would be monitored. There are a number of limitations to the measurement of adherence used in this and similar studies. It may be difficult for caregivers to recall such details over a two week period, or they may deliberately mis-report tablet consumption if they are concerned about revealing inappropriate dosing. In formal health structures such as government health facilities the child's weight as opposed to age may be used to determine the dose (Njogu *et al.,* 2008), so children who did not fall into the standard weight range for their age may have appeared to have obtained the wrong number of tablets. However, given these provisos, there was no evidence that retail provision of AL led to an increase in poor AL use. There was no difference between adherence to Tibamal® (received entirely from retailers) and other AL brands (received mainly from facilities), and no significant difference was observed in the accuracy of AL doses overall obtained or consumed between the control and intervention arms at follow-up. In fact there was some indication that the probability of a child receiving the correct dose was higher at follow-up in the intervention area (67%) than in the control area (49%). However, there remains room for improvement in adherence to AL obtained from all sources, as even at follow-up in the intervention area around a third of children were not consuming the correct dose. Reasons for this may include poor knowledge of dosing regimens, lack of advice from providers, and stockouts of one of the AL pack sizes meaning that children may have been sold an inappropriate pack for their age. During FGDs carried out by Kedenge (2011) caregivers also reported stopping medication as soon as the fever subsides, and believing that the child's recovery would hasten if all the tablets were given at more frequent intervals than stipulated in the dosing regimen. Interventions to improve adherence could include reducing stock-outs of specific pack sizes, encouraging shopkeepers to talk through the package dosing instructions with caretakers, and the use of mass media to emphasise the importance of completing the full dose (Yeung & White, 2005).

There was also room for improvement in the advice given to caregivers by retail staff on AL. Just under half of caregivers reported receiving advice from specialised drug store staff on how to administer the medicine. In contrast up to 70% of caregivers reported receiving dosing advice from general stores. Hardly any caregivers reported any advice on what to do if the child vomits, or which foods to give with AL. However, it should also be noted that qualified health workers often also perform poorly on the provision of such advice, as noted in Chapter 5. In a health facility survey carried out in Kenya, only 38% of health workers gave advice on administering AL after a meal and only 8% on what to do if the child vomited after taking AL (Zurovac *et al.,* 2008)

Although Tibamal® was targeted at children 3 to 59 months, a significant minority of adults and children above this age band reported taking the drug to treat a fever in the intervention arm. Moreover, it is likely that Tibamal® use in older age groups may have been under-reported if respondents were aware that only younger children were supposed to receive this drug (Kedenge, 2011). No children less than 3 months with fever received Tibamal®.

Finally, a number of potential limitations to the household survey results should be borne in mind. Contamination was very minimal with only 7% of caregivers in the control arm having heard of Tibamal® at follow-up, and none reporting having purchased it to treat their under five child. However, the study is likely to have faced other limitations common to such surveys including problems of recall and potential social desirability bias (respondents may report what they believe to be appropriate behaviour rather than what they actually did). Further limitations that apply to the evaluation in general are discussed in chapter 8.

Summary: In summary, the main finding of the household survey was that the intervention was able to significantly increase the percentage of children receiving AL treatment on the same day or following day to more than double the coverage observed in the control arm at follow-up, and this effect was also demonstrated among the poorest in the community. Observations possibly contributing to this finding included that the subsidised Tibamal® resulted in increased competitiveness of this treatment compared to other monotherapies, and a tendency for those using some kind of antimalarial monotherapy at baseline to substitute it for Tibamal®. Over 95% of caregivers in the intervention arm who purchase Tibamal® purchased it at the recommended price of 20KSH. Furthermore, the intervention was able to significantly increase caregivers' awareness of the treatment and bring the treatment physically closer to the community. The intervention did not deter caregivers from healthcare facilities, but instead influenced those who usually bought treatment for fever from a retail outlet to purchase AL. The intervention had no significant impact on the proportion of children receiving or adhering to the correct dose of AL treatment nor was there any significant improvement in the percentage of caregivers receiving appropriate counselling advice on how to administer the treatment and what to do if the child vomits or does not get better.

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CHAPTER 8

DISCUSSION & CONCLUSION

8.1: INTRODUCTION

ACTs are generally accepted as the best treatment for uncomplicated malaria, however access to this treatment remains low. One way of improving access is through HMM. According to the RBM partnership, HMM strategies should aim to overcome barriers to accessing effective malaria treatment and improve quality of care received by working with both the formal and informal services offered within communities, outside of clinical settings.

One possible strategy is to roll out HMM using existing medicine retailers. Due to the high free market prices of ACT, this strategy requires drug subsidies to ensure wide coverage. Kenya is in the process of rolling out such an approach in the private sector, supported by the AMF-m framework which provides a co-payment directly to preselected manufacturers of ACTs, in order to reduce the price of this treatment to first-line buyers. However, there is limited evidence to guide this process or similar subsidy strategies, with certain questions regarding this roll out strategy remaining unanswered. These include, with only a sub set of the community using retailers, will an HMM intervention targeting this sector have significant impact on coverage; will a brief training of providers be able to change their behaviour; will providers be willing to pass on a subsidy to consumers or will they be more inclined on retaining the original treatment price in order to maximize profits; and what barriers may providers experience that may prevent them from stocking the subsidised treatment. It is also not known whether community awareness activities will be sufficient to improve consumer treatment seeking behaviour and whether such an intervention will reach the poorest, who would most benefit from better access.

The purpose of this thesis is to provide some insight into these questions by evaluating the provision of pre-packaged subsidised AL treatment, provided to trained retail outlets with community awareness activities to stimulate consumer demand. The intervention was evaluated using a cluster randomised controlled design, with data collected at baseline and 8 months post-intervention.

In this chapter, I will first evaluate the general study strengths and limitations. In section 8.2 I will bring key findings together from the previous chapters to see how they have informed the objectives of the study, and assess how external factors may have affected the study outcomes. In section 8.3 I will go on to describe the policy implications of the study and in section 8.4 conclude by reviewing the next steps, beyond this thesis.

8.2: General Strengths and Limitations of the Study

8.2.1: Strengths

According to the Roll Back Malaria partnership, the ideal HMM strategy should have three components, an effective communication strategy; training of community based providers on the skills and knowledge necessary to deliver adequate healthcare; and a guaranteed supply of high quality pre-packaged anti-malarial medication (RBM, 2005). The HMM intervention in this evaluation was designed to contain all these components and therefore allows for one to determine outcomes that can be achieved through the implementation of such an optimum intervention.

This study also addresses some of the knowledge gaps identified from reviews carried out on available HMM intervention studies as discussed in Chapter 2. It has been argued that most studies limit their indicators to intermediate outcome measures such as provider knowledge and behaviour rather than those more closely linked to health outcomes. Although this study did not assess the effect of the intervention on mortality and morbidity, the impact on community drug use was evaluated, which is in line with the RBM target of improving coverage of effective treatment. Few studies evaluate the outcome of their intervention in different socio-economic groups. This is something that has been evaluated in this study and allows for one to interpret if the coverage of the intervention was equitable and reached the poorest of society, who are in most need of improved access to treatment. More generally, many reviews comment on the few studies available that evaluate HMM interventions in the private retail sector, and literature on ACT subsidies in the private sector is especially limited. This study increases the pool of available evidence on this topic, and is the first study to assess the impact of ACT subsidies on ACT coverage at the community level.

Several reviews have documented the challenges of drawing firm conclusions about strategies to improve retail sector treatment provision due to studies often having weak designs such as lacking adequate controls (Goodman *et al.,* 2007; Smith (b) *et al.*, 2009; Wafula & Goodman, 2010; Hopkins *et al.,* 2007; Smith (a) 2009). In order to address weaknesses observed in previous study designs, this study was evaluated using a cluster randomised controlled design, comparing pre and post data to significantly reduce the influence of chance, bias, or confounding due for example to variations in public sector drug stocks, weather patterns and malaria awareness campaigns (Habicht *et al.,* 1999; Vandenbroucke, 2008; Victora *et al.,* 2004; Atkins, 2007). This improves the accuracy in interpreting the effects of the intervention. Also, the designs of previous HMM interventions do not allow for comparability across studies mainly due to different outcome indicators being monitored from one study to the next. In order to ensure indicators selected could be compared to other similar studies in Kenya, and to ensure relevant policy issues were addressed, a stakeholder meeting was held during the initial stages of this study design. Stakeholders included the Ministry of Health, DOMC, the pharmacy and poisons regulatory body (PPB), PSI (members of the implementation team), KWRT (the evaluators of the intervention), and other organizations that have either carried out or are interested in carrying out similar studies such as the Kenya Red Cross and SHEF. The purpose of the meeting was to formulate a list of indicators to be used across all HMM studies in Kenya. The indictors were collated from DOMC targets, GF and RBM Monitoring and Evaluation Reference Group (RBM MERG M&E) frameworks, and the draft monitoring and evaluation (M&E) guidelines for the global ACT subsidy. The indicators used in this study were derived from this list. Involving important stakeholders such as the DOMC and the PPB from the beginning of the study was important in ensuring the success of implementing and evaluating the study intervention. Apart from approving the study indicators, the DOMC played an important role in determining the direction and design of the study. The DOMC also designed the training materials for retailers and attended training sessions. The PPB played a significant role in ensuring PPB regulations were adhered to. This was important since having AL available in retail outlets was potentially a very sensitive issue requiring expert pharmaceutical guidance. In the field, MOH staff and leaders of the community were informed and gave consent for the study to take place. At the end of the study, the main study outcomes were then disseminated to the relevant ministry of health staff both at headquarters in Nairobi and also to the Provincial and District staff from the study sites. As described in Chapter 3, this involvement helped in stakeholders having ownership of the study and impacted on its acceptance and ability to inform national malaria policy.

Having three different data collection activities in one study is another strength. The weaknesses of one data collection activity can be supported by the strength of another. For example in the provider survey, interviewees knew that they were being interviewed and therefore may have given responses that they felt were appropriate but were not necessarily true. The validity of the responses could be confirmed through the mystery shopper survey where interviewees were unaware that they were being surveyed. Data from one activity can therefore be used to support findings from another, enhancing the reliability of the findings.

8.2.2: Limitations

Specific limitations for each data collection method are highlighted in the relevant results chapters. In this section the limitations of the overall study design are considered.

While randomised controlled trials are argued to have high internal validity, there is concern that they may lack external validity because the study design demands implementation practices that would be unrealistic in operational settings, as described in Chapter 3. In this study, the HMM intervention was designed as much as possible to mimic what would happen in a typical, real life scenario. However, to avoid contamination of control sub-locations, consumer education had to be controlled, meaning that mass media techniques such as radio and TV spots could not be used. In addition, the delivery of the drug had to be made directly to trained outlets. Both these methods of implementation would not be feasible on a larger scale where it would be more practical and efficient to use mass media campaigns, and take advantage of the usual drug supply chains. On the other hand, stock outs of the intervention's treatment were observed, indicating that the implementation team were not able to ensure 100% delivery of the intervention and adherence to its recommendations by providers. In fact, it is possible that stockouts would have been rarer without direct delivery, as shopkeepers would have had wider choice of suppliers of subsidised ACT. This places the study in the category of 'public health programme efficacy', described by Victora *et al.,* (2004) (see Chapter 3), where the delivery mechanism and the compliance to its recommendations are at the level of 'best practice' as opposed to the extremes of being 'ideal' or 'routine'. The outcomes of such a study look more at the efficacy of the intervention (i.e. which aims to show whether the intervention can produce the desired outcomes under ideal conditions) as opposed to programme effectiveness where the intervention is implemented with no additional efforts made to ensure delivery or dose uptake (under 'routine' conditions), resulting in outcomes that are more likely under 'real life' conditions. This means that the results may to some degree overestimate the impact that would be seen under routine conditions.

Two other factors that may limit the strength of the study design are the process of randomisation and blinding. A modified randomisation process was used to select sub-locations in order to reduce the potential for contamination. The creation of a buffer zone around selected sub-locations meant that sub-locations meeting the selection criteria did not all have an equal chance of being selected for the study. Baseline data from the studies however indicate that control and intervention arms had similar characteristics. Additionally due to the design of the community awareness activities, it was not possible to blind the participants or data collectors. The presence of Tibamal® promotional items such as wall paintings and *barazas* made it obvious which sub-locations were in the intervention arm and which were in the control arm. Knowing which arm one was in may to some degree have influenced the responses given by interviewees or recorded by field staff or their actions. For example, in the provider survey, a provider in the control arm who is aware of the counselling advice of AL may not feel as pressurised to give full details of his knowledge as a trained provider in the intervention arm selling Tibamal® who may be scared of the possibility of being blacklisted by PSI. Similarly a caregiver in the intervention arm may be more aware that AL is the appropriate treatment and therefore subject to stronger social desirability bias to state that they used AL even if they did not. This may have artificially enhanced the positive impacts of the intervention recorded.

There are also limitations observed in reviews looking at HMM studies that also apply to this study. A cost-effectiveness analysis could not be carried out mainly because any data on costs may have been overestimated due to the need to deliver drugs directly to retail outlets, and the small scale of the pilot which meant that economies of scale could not be exploited. Also, it was hoped that the period between implementation of the intervention and follow-up data collection would be close to 12 months, to allow for one to judge the sustainability of the observed outcomes. However, the delay in gaining approval from the PPB on deregulation of AL meant implementation was delayed, reducing the period between implementation and evaluation to 8 months after Tibamal® distribution began and 4 months after the start of community awareness activities. It is not known if with time caregivers forget the community awareness activity messages and therefore demand less AL, or if caregivers may become more used to and positive about the product, increasing its demand. Similarly providers may with time forget the knowledge gained in training, reducing the impact of the intervention on the quality of services received by the provider. Lastly, it was not possible to assess the impact of the intervention on the potential development of ACT resistance, which could be a cause of concern as the intervention did substantially increase ACT use, with adherence to full treatment doses being far from optimal.

8.3: DISCUSSION OF KEY FINDINGS

The primary objective of this study was to evaluate to what extent the provision of pre-packaged, subsidized, AL delivered through private sector retailers would improve the coverage of prompt effective anti-malarial treatment. The household survey showed that the intervention was able to significantly increase the percentage of children receiving AL treatment on the same day or following day of fever onset by 25% points. This was more than double the coverage observed in the control arm at follow-up. There are many possible factors that could have contributed to this increase in AL coverage.

The one day training of providers was able to improve their knowledge on malaria treatment and diagnosis and opinions of ACTs. The provider survey showed a significant increase in the percentage of providers having heard of Tibamal®, the intervention's branded AL, by 78% points, when the intervention arm was compared to the control arm at follow-up. The same survey showed a 24% point increase in those knowing that AL was the recommended first line treatment for uncomplicated malaria, and by follow-up 80% of outlets in the intervention arm thought that AL was more effective than other antimalarial treatments. The training also seemed to have an effect on provider behaviour. The mystery shopper survey showed that a significantly larger percentage of providers prescribed AL for the treatment of fever in a four year old child when the intervention arm was compared to the control arm, at follow-up. Providers were also able to pass on the treatment subsidy to caregivers, selling Tibamal® at the recommended retail price of 20KSH. This was observed in both the household and mystery shopper survey where over 90% of purchased Tibamal® was bought at the recommended retail price. The subsided price was calculated to make AL as affordable as other more commonly used, but less effective antimalarial monotherapies. Passing on the subsidy to caregivers made the treatment as price competitive as other more popular antimalarial monotherapies. The increased competitiveness of the subsidised Tibamal® compared to other monotherapies was observed in the household survey which showed a tendency for those already using some kind of antimalarial monotherapy at baseline to be more likely to substitute it for Tibamal® at follow-up. Apart from cost, the intervention was able to improve the availability of Tibamal® in retail outlets, bringing the treatment physically closer to the community. The provider survey showed that at follow-up, the supply of Tibamal® significantly increased the percentage of outlets stocking any kind of AL brand by 32% points when the control arm was compared to the intervention arm. This resulted in a significant decline in household travel time to the nearest retail source of AL, by walking, from around half an hour in the control group to ten minutes in the intervention arm.

Caregivers' knowledge of malaria and treatment behaviour appeared to also have been positively affected by the intervention. The household survey showed a 75% point increase in the percentage of caregivers having heard of Tibamal® in the intervention arm compared to the control arm, at follow-up. Most of the information regarding Tibamal® was reported to have been sourced by word of mouth from healthcare staff and 'other people', who would have most likely seen a poster, wall paintings and packaging of the product or attended one of the community activities which included *barazas*. Part of the significant increased uptake of AL could be attributed to the success of the community awareness activities in increasing caregivers' awareness of the treatment, and as a result generating consumer demand for the product. This seems to be important since the provider survey showed that consumer demand was by far the greatest factor that influenced what treatments providers stocked and sold to consumers. The household survey also showed that the intervention did not deter caregivers away from healthcare facilities, but instead influenced those who usually bought treatment for fever from a retail outlet to purchase AL.

Although data from the household survey showed that coverage of AL had significantly improved, it still fell below the 80% target set by the RBM. Two factors directly linked to the intervention could possibly explain the limits to the impact observed. Firstly, at follow-up, only 43% of all possible outlets that conformed to the selection criteria and could have supplied Tibamal® had been included into the intervention, limiting the availability of the treatment. Reasons given by PSI for this relatively low uptake of the intervention have been discussed in Chapter 5 and include that some outlets identified for inclusion were unable to attend the training due to other commitments or were closed when invitations to attend the training were being given. Even after receiving training some outlets may have changed the type of business they were running and stopped selling medication, closed up their business, or relocated to outside the study area. Other trained outlets were given the opportunity to buy and stock Tibamal®, but were unable to because they did not have the funds to purchase the treatment from the sales staff. Secondly, stock outs of AL within two weeks prior to the survey were reported in 33% of outlets in the intervention arm at follow-up. This stock out could have also reduced the availability of AL within the communities, and may have impacted negatively on the percentage being treated with AL. Careseeking patterns may also limit the increase in treatment coverage. Some fevers are not treated with any antimalarial with or without the interventions, because caregivers perceive them as very mild or as having another cause, or because they cannot afford even the cheapest antimalarial on the market. In these cases, it may be much harder to shift caregiver behaviour to the use of ACT.

One of the specific objectives of the study was to determine the distribution of the benefits of retail sector delivery of AL by socio-economic status. The household survey was able to demonstrate that there was no correlation observed between increasing wealth and the probability of receiving AL. This indicates that the benefits of the intervention were equally spread throughout all socio-economic classes. The intervention was therefore able to reach the poorest in the community who are the least able to access effective malaria treatment and would therefore be the most likely to benefit from such an intervention. This finding should however be interpreted with some caution. One of the potential weaknesses of using asset-based measures to measure socio-economic status in this rural part of Kenya is that many households tend to have similar durable items, access to utilities and infrastructure. This exposes the data to the problem of clumping (as described in appendix 4) making it difficult to differentiate between poor and very poor households (Vyas & Kumaranayake (2006)). Other studies looking at the impact of subsidising ACTs on access across different socio-economic groups had varied findings. One study also carried out in Western Kenya showed that an ACT subsidy more than tripled the treatment's use by illiterate-headed households, which were classified as the poorest households, while the impact on literate households was much less (Cohen *et al.,* 2011). A study in Tanzania showed ACTs tended to be stocked more often in shops frequented by individuals of higher socioeconomic status (Cohen *et al.,* 2010), and in Uganda, ACT market share was lower among those in the lower socioeconomic status groups (Schäferhoff & Yamey, 2011).

Other specific objectives of the study were to determine the impact of the intervention on the proportion of children being treated appropriately and adhering to the correct dose; and to determine if private sector retailers can deliver AL to appropriate standards of quality. Adherence was measured as reporting consumption of exactly the correct number of tablets for the child's age within three days of receiving the medication. To be able to adhere to the correct dose, caregivers needed to have received the correct dose from the provider. The household survey showed that an average of 75% of caregivers across both arms at follow-up that received AL received the correct dose for their child's fever from a retail outlet. The intervention seemed to have no effect on this as there was an insignificant difference observed between the arms. This is not in line with what was observed in the mystery shopper survey, where more than 90% of caregivers received the correct dose for their child at follow-up. The difference in percentages observed between the surveys could have been due to the different data collection methods. In the household survey, caregivers were able to access treatment from their choice of provider. If one of the providers dispensing the wrong dose was being accessed by many caregivers, this would have had a negative effect on the percentage of caregivers receiving the correct dose. However, in the mystery shopper survey all outlets were only interviewed once, reducing the impact of such a provider on the outcome. Also, the scenario presented to the provider in the mystery shopper survey ensured that the age of the child was mentioned. In the household survey, it was up to the provider to ask the age of the child. It could be that some providers were complacent, forgetting to ask the child's age and dispensing the AL pack that was either available in the outlet (if the other had gone out of stock) or randomly selecting one of the two packs to dispense, regardless of the child's age. Another reason could be due to the price of non-intervention AL. It could be that some caregivers were unable to afford the full dose of the unsubsidised AL in outlets where Tibamal® was not available, therefore only purchasing the number of tablets that they could afford, even though it was insufficient for their child. By contrast mystery shoppers had sufficient funds to purchase a complete does of whatever was suggested by the provider. Other reasons given for providers in the household survey not giving the correct dosage to the caregiver are discussed further in Chapter 7.

It seems from the household survey that the percentage of children adhering to AL treatment remained unchanged post-intervention. One possible explanation for this is linked to relatively low levels of appropriate dosing advice given to caregivers. The household survey showed 35% of specialised drug outlets were reported to have correctly counselled caregivers on how to administer the treatment, and just under half of all outlets provided the correct dosing information in the mystery shopper survey. The provider survey revealed that after training of providers, only 13% of respondents in the intervention arm knew the correct dosing advice for a four year old child suffering from fever. All this is despite the provision of job aids providing guidance on dosing in some trained outlets. However, it should be noted that the percentage of outlets with job aids was extremely low, found in only 22% of all outlets in the intervention arm. Information from the FGDs may also help in revealing why trained providers do not counsel all patients they dispense AL to. Majority of retailers, especially those from general stores, stated that in many instances, they would "have many customers to attend to" and hence not have "time to discuss with a patient to satisfaction" (Kedenge, 2011).

Passing on the correct dosing information to the caregiver may not necessarily result in 100% adherence of recipients to the treatment as sometimes caregivers ignore the advice given to them. A review carried out on interventions designed to improve adherence to antimalarial treatments showed that pre-packaging of treatment, the use of blister packaging, giving patients both verbal and pictorial instructions on how to administer the medication, training providers on the correct counselling advice while providing job aids to help in dispensing the correct dose, and community education to encourage adherence have all shown positive results (Yeung & White, 2005). Many of these activities were implemented in the intervention however no significant improvements were observed at follow-up. This may be due to many factors. The AL available in government facilities at baseline (the most sourced AL at baseline) was already in a blister pack and had some pictorial diagrams on the packaging on dosing advice. It is worth questioning if the additional pictorial diagrams added onto the intervention's packaging had any additional effects to adherence. Also, patients from healthcare facilities should be routinely counselled on how AL is to be administered. It could be that the percentage of recipients being counselled on AL in retail outlets remained similar to those in government health facilities, post-intervention. The FGDs could also provide further insight into obstacles caregivers experience, causing them not to adhere to the dosing guidelines, despite the intervention's community awareness campaigns.

Another objective was to determine if private sector retailers can deliver AL to appropriate standards of quality for the treatment of fever in children under five years. In addition to providing the correct dose as described above, 'appropriate standards of quality' consists of adequate counselling advice being given by the provider on issues concerning AL, and appropriate storage of AL to maintain its efficacy. The quality of counselling advice has been briefly discussed in the above, when looking at dosing advice, which showed that there is still room for improvement on the percentage of providers counselling on how to administer AL. Apart from the dose that should be administered to the child, other counselling advice that should be given by retailers are what to do if the child vomits after taking the treatment, what to do if the child does not get better and what foods to give the child. The provider survey showed that although the intervention did improve knowledge on counselling advice, there was considerable room for improvement. Overall the greatest change in knowledge was observed with 66% of respondents in the intervention arm at follow-up knowing the correct advice on what to do if the child does not improve. This was a 17% point difference from baseline. The mystery shopper survey revealed similar results, with most providers giving appropriate advice at follow-up in the intervention arm, on what to do if the child does not get better, however this remained below 35%. As already discussed in Chapter 7, healthcare workers also perform poorly on provision of AL counselling advice. A study carried out by Zurovac *et al.,* (2011) showed that regularly sending reminder text messages to healthcare workers' phones on good counselling practices can significantly improve the percentage of malaria patients being correctly managed.

The provider survey was able to assess the storage of AL. AL was to be stored off the floor, out of direct sunlight, in a dry area and with the packaging intact. At follow-up over 80% of outlets were storing AL according to these requirements, however it seems that this had little to do with the intervention since there was an insignificant difference when compared to those storing AL appropriately in the control arm. The provider survey also revealed that less than 1% of outlets had expired stocks of AL in both arms at follow-up.

The context analysis data were able to highlight potential external factors that may have influenced the study outcomes. A table of all contextual factors identified is presented in *appendix 10*. Although it is not possible to assess the quantitative impact of these influences on the study outcomes, of all the factor identified, two main factors likely to have had a significant impact on the study outcomes: the issuing of a government directive to halt the production and supply of less effective monotherapies; and the erratic AL supplies experienced in government health facilities. During the study period, the MOH PPB circulated letters to all importers, manufacturers, wholesale dealers, distributors and retailers, restricting the manufacturing, supply and sale of artemisinin monotherapies, SP and amodiaquine by the end of 2008. This was enforced by inspection teams visiting outlets and shutting down those selling medications illegally. The provider survey shows that at baseline 50% of outlets stocked amodiaquine and this decreased to below 20% at follow-up, and communication with a predominant amodiaquine manufacturer confirmed it had terminated its production of the drug. Although this activity was not part of the intervention, and would have affected control and intervention areas in the same way, it created an enabling environment for the intervention to be implemented. This directive is likely to have reduced the availability of some antimalarial monotherapies such as SP and amodiaquine, decreasing competition between AL and these treatments and hence facilitating the increase in AL's market share when the subsidy was introduced, and the increase in coverage observed in the household survey.

Since the introduction of free AL into government facilities, supplies of AL in this sector have experienced fluctuations, with periods of very low stocks alternating with periods of average or good stock levels (Kangwana *et al.,* 2009; DOMC 2010; Amin *et al.,* 2007). During the baseline survey, AL stocks within government health facilities in the study areas were extremely low (*appendix 9*). This period of low stocks was experienced nation-wide, and had been caused in large part by delayed government procurement of the treatment (Kangwana *et al.,* 2009). The poor availability of AL is likely to explain the low percentage of caregivers accessing this treatment at baseline. AL levels had picked up by follow-up, and this may have contributed to increased usage of the treatment reported by caregivers, however this would have affected both the intervention and control arms.

In summary, this study shows that the intervention was able to improve coverage of effective antimalarial treatment, including to the poorest in society. It also improved knowledge of providers and caregivers, and accessibility and affordability of ACT. However, the intervention was unable to impact on the level of appropriate counselling delivered by retailers or adherence practices of recipients of the treatment.

Only 21 studies were identified as having evaluated the impact of HMM interventions in improving access to effective antimalarial treatment through the private retail sector, using similar indicators (refer to chapter 2). As discussed in Chapter 2, there are limitations in comparing other study findings to the ones reported here, including the diversity in HMM strategies being evaluated, with no two strategies being the same; variations in the time period between implementation of the intervention and evaluation of the study outcomes; few studies carrying out hypothesis testing making the significance of any changes hard to interpret; and many studies having poor study designs such as a very low sample size or having no comparison group, exposing the results to potential bias. However, some general comparisons can be made. Studies in Tanzania and Uganda showed that subsidising ACTs led to their rapid uptake and a decrease in the use of antimalarial monotherapies, with good adherence to recommended retail prices (Talisuna *et al.,* 2009; Sabot *et al.,* 2009; Sabot *et al.,* 2008. In Tanzania there was a 53% point increase in consumers purchasing antimalarials for a child under five in the intervention arms compared to a 6% point increase in the control arm (Sabot *et al.,* 2008). In Uganda there was a 55% point increase in subsidised ACTs purchased from a licensed drug shop for children under five years old (Talisuna *et al.,* 2009). In both countries the price of subsidised ACTs remained comparable or below the price of sub-optimal antimalarials. By contrast studies in Cambodia and Senegal showed that ACT subsidies had no significant effect on ACT availability, which remained low in both countries and irregular in Cambodia. In Cambodia after one year of supplying subsidised ACTs, only 6% of private retail outlets stocked children's doses and in Senegal only 43% stocked children's doses (Sabot *et al.,* 2008). The poor market penetration in Cambodia was associated with retail prices above the recommended retail prices. No other published data are yet available on the impact of private sector ACT subsidies on coverage of prompt effective treatment, and robust data on other strategies to improve ACT coverage are limited. There is however evidence that provision of ACTs through CHWs could also lead to high levels of ACT coverage, with a multicountry study in Ghana, Nigeria, and Uganda finding that 59% of children reporting fever in the past two weeks had received an ACT from a CHW (Ajayi *et al.,* 2009). Two studies contained IEC components as part of their HMM intervention. One IEC strategy in Zambia involving the use of trained village health motivators and vendors educating mothers (Kaona & Tuba, 2003), and another in Cambodia, using mass media campaigns (Sabot *et al.,* 2008) were able to improve caregivers' knowledge on malaria (Kaona & Tuba, 2003; Sabot *et al.,* 2008). Studies evaluating the effect of training of retail outlet providers to improve their knowledge and behaviour on malaria and its treatment have mostly shown positive findings (Kaona & Tuba, 2003; Sabot *et al,* 2008; Oshiname & Brieger, 1992; Tavrow *et al.,* 2003; Gilpin *et al.,* 2006; Greer *et al.,* 2004; Muturi, 2001; Abuya *et al.,* 2009; Nsimba, 2006; Marsh *et al.,* 1999; Marsh *et al.,* 2004; Twafik *et al.,* 2006). Most of these studies showed training having a higher impact on provider knowledge and behaviour when compared to the study discussed in this thesis. This could be due to a variety of factors including some interventions having a relatively short time period between training and evaluation; some interventions incorporating regular monitoring and supervision of providers post training; and some interventions having longer training sessions or the training sessions being more involving, either by being on a one on one basis or tailored to be less didactic (refer to the 'negotiation sessions' discussed in Chapter 2).

Lessons learnt from studies carried out on the impact of subsidising ACTs in the private sector have shown that on a national scale such an intervention will likely only have modest changes on ACT price, availability and market share; that it is questionable whether such subsides will increase ACT usage on a national scale, and that ACTs may still remain out of reach to the poorest in society (Schäferhoff & Yamey, 2011).

8.4: POLICY IMPLICATIONS

A key policy implication of this study is that the type of intervention implemented, involving subsidised pre-packaged ACT, together with training and IEC activities, is potentially an important tool in increasing ACT coverage. The findings also allay to some degree some concerns that had been expressed about subsidising ACT in the private sector. For example, some stakeholders had been worried that providing effective treatment outside of formal health facilities would deter patients away from this sector to the private sector. Our study showed no evidence of this type of migration during the period between the roll out of the intervention and follow-up data collection activities. Secondly, some have argued that releasing ACTs into the private sector may increase it misuse, with private sector customers being much less likely to adhere to treatment doses. However, in this study adherence to treatment received from the retail sector was similar to that from health facilities. Thirdly, there have been fears of private suppliers engaging in "price gouging" where they fail to pass on the subsidy to the consumer, but in this case adherence to the recommended prices was good. A final concern is that even with the subsidy, the intervention may not reach the poorest groups. This study has shown that such subsidies can benefit all socio-economic groups in poor rural communities.

However, the study also points to several areas where further work on intervention design is required, particularly around poor counselling advice. This may have been a reflection of lack of improvement in knowledge on how to dispense the medication despite providers having undergone training and a lack of incentives for retailers to spend time providing advice when they will not benefit from it financially and may have many customers. Additional interventions are also clearly needed to improve adherence for both facility and retail careseekers. At the provider level this could be improved through provider refresher training, continuous supervision and ensuring that a high percentage of outlets receive dispensing job aids. At the caregiver level, adherence might be improved by enhancing the instructions on packaging and by more intensive IEC activities.

However, in using these results to develop policy recommendations a number of issues should be considered. First, care must be taken in extrapolating these findings to other areas or even to a national scale. The study was undertaken in three districts only, all within one province in Kenya, and was restricted to rural areas. In some respects these districts can be considered relatively representative of the region and to some extent Kenya as a whole. Recent national data in the lake endemic region showed fever prevalence was 41%. Of those fevers 40% received an antimalarial, 24% received an ACT and 16% received this ACT on the same or next day of fever developing. Of those who had treatment sought for their fever, 36% received it from the private sector (private health facilities, pharmacies and shops). Only 10% of fevers had blood samples taken for malaria testing. Across Kenya as a whole national data showed an average of 35% of fevers being treated with an antimalarial 18% receiving an ACT, 11% receiving it on the same or next day, 33%% receiving treatment from the private sector and 12% having a blood sample taken for a malaria test (DOMC, 2011). Data from this study showed fever prevalence to average 29%, antimalarial use at 50%, AL use at 27% and AL use the same day or following day this was 20%. Care sourced from the private sector was slightly over 44% and only 9% of children were reported to have had a malaria test done. ITN use and education levels reported in this study are also similar to those reported in national surveys (MIS 2010; DOMC, 2009); 58% of households in the control arm and 60% in the intervention arm were classified as poor, compared to a national average of 54% (CBS 1999). However unlike many regions in Kenya, the study areas have very high levels of malaria endemicity compared with the rest of the country, and a relatively active retail drug market, with many specialized drug stores. Reasons for limiting the study to such a setting have been explained in Chapter 4 'Study Design and Methodology'. The characteristics of the study sites may have influenced treatment seeking behaviour and provider practices in these areas. The effects of these characteristics have been described in Chapter 2. For example, in malaria endemic areas, where people are more familiar with the symptoms of malaria, self-treatment may be more common than other forms of care. Having an active retail market may also be indicative of a high level of self-treatment. If this is true then one would expect the intervention to have a greater impact in such areas since it targets a large source of treatment in the retail sector. On the other hand, one would expect the intervention to have less impact in areas where public sector AL supplies are good, although reliable drug supply chains are not common in sub Saharan Africa. The area of residence has been shown to influence treatment seeking practices. Whether rural or urban, the location of residence may be an indicator of more fundamental factors such as beliefs in different types of treatment, ease in accessing different healthcare sectors or be a reflection of socio-economic status. Assuming rural areas are linked with poorer SES, one would expect reducing the cost of treatment through a subsidy to have a more positive impact on its coverage than in better off areas. However, in poorer areas there may be more people who cannot even afford the subsidised price of AL, meaning that the intervention could have a greater impact in better-off settings. On the other hand, in other areas the intervention could have additional benefits in the form of crowding out artemisinin monotherapies, reducing the potential for artemisinin resistance to develop. This advantage was not apparent in this setting as use of artemisinin monotherapies was so low at baseline, but would be important in areas where artemisinin monotherapies have a significant high market share such as Nigeria, the Democratic Republic of Congo, and Cambodia (O'Connell *et al.,* 2011; O'Connell, 2009). In sum, the impact of the study intervention in these areas may therefore be different to other areas with different environments and therefore practices and the generalisability of the results to other areas should be carefully considered. However, the results are likely to be applicable to many rural settings where use of drug retailers is high.

The study results could be considered as a positive indication of the potential impact of AMF-m. However, there are a number of differences between this pilot and the AMF-m roll out, meaning that the results should be used with caution for predicting AMF-m impact. Under AMF-m subsidised drugs will be distributed through existing private and public sector distribution chains. By contrast, as described above, Tibamal® was distributed directly to retail outlets in order to avoid contamination of control areas; it is possible that use of existing private sector distribution chains may either improve or worsen retail sector availability, and the likely impact on final retail prices is unclear. This intervention was targeted at children under 3-59 months only, but under AMF-m subsidised drugs will be available to all age groups. No mass media promotion was used in the pilot, again to avoid contamination, though this is supposed to be a major feature of AMF-m roll out, potentially enhancing provider knowledge of malaria symptoms, treatment and consumer demand. This pilot included all medicine retailers including general stores however, most countries planning to implement AMF-m intend to restrict the availability of subsidised AL to registered pharmacies and in some cases drug stores. In Africa, Ghana and Nigeria deregulated the classification of their ACTs to an OTC medication. Other countries such as Madagascar, Uganda, Niger and Kenya have maintained the classification of their ACTs as POM. It is unclear how such a narrower range of retail outlets will have similar outcomes on AL access, provider knowledge and behaviour. Further analysis of these data by retail type do show that there are differences in key outcomes such as AL availability, price and counselling advice between general stores and specialised drug stores in the intervention area, with specialised drug stores being generally better stocked and more knowledgeable on counselling advice, but having less competitive prices than general stores (*appendix 5*). However, this study shows that although at baseline general stores tended to perform worse than specialised drug stores, the improvement in practices such as asking for danger signs, dispensing of antimalarials and dispensing of AL seemed to be greater in general stores than specialised drug stores, indicating that general stores benefited more from the intervention than specialised drug stores.

In Kenya AMF-m drugs are supposed to be restricted to registered pharmacies. Registered pharmacies are extremely rare outside of towns in Kenya, implying that either the impact on rural ACT availability will be very limited, or that subsidised ACT will leak to other drug retailers who will not, however, have received any AMF-m related training, which could compromise quality of dispensing.

The first co-payments for Phase I of AMF-m were made in August 2010, to Ghana and Kenya. Phase 1 is planned to run until December 2012, when it will be reviewed to assess whether it should be continued. An independent evaluation will assess the impact of AMF-m on affordability, price, use and market share of effective malaria treatment using a before and after study focused on outlets and documentation of context. Baseline outlet (provider) surveys were carried out in all AMF-m pilot countries in late 2010, with follow-up surveys planned in late 2011. While this evaluation has the advantage that it will be studying nationwide roll-out under operational conditions, it also faces a number of limitations. The inability to find appropriate comparator countries and limited financial resources meant that the intervention will be evaluated using a probability instead of a plausibility design (refer to Chapter 3). The effect of AMF-m on ACT use will be derived from secondary data from national household surveys such as the DHS, however these may not be timed appropriately for the AMF-m evaluation. The time between initial roll out and endpoint evaluations may also be considered too short to evaluate the long term effects of AMF-m as full nationwide rollout could take much longer than that for small scale pilots (Macro & LSHTM, 2010). For these reasons, the findings of the Tibamal® study are still likely to be useful to policy makers even once the AMF-m independent evaluation results are available.

The thesis results also need to be considered in the light of other current policy debates. At the start of this study, WHO recommended that all febrile children under five years living in malaria endemic regions should be treated presumptively with effective antimalarial treatment. The RBM monitored this recommendation by setting country targets of an 80% coverage of appropriate antimalarial treatment within 24 hours of fever onset (World Malaria Report, 2008). The HMM intervention described in this study was able to significantly increase the percentage of children being treated presumptively with effective anti-malarial treatment, although coverage did not reach the 80% target suggested by the RBM partnership. This RBM target has since been amended to achieving universal coverage (RBM, 2008).

International policy is now leaning towards diagnostic confirmation of all suspected malaria cases prior to treating. As a result some stakeholders feel that interventions such as the Tibamal® one to improve ACT coverage should only be implemented where they can be accompanied by expanded access to diagnosis. The introduction of diagnostics into the private retail sector alongside subsidising ACT has its advantages. Targeting anti-malarial treatment to those who would benefit from it will in turn reduce the numbers unnecessarily exposed to the potential side effects of the treatment; potentially improve the cost-effectiveness of malaria treatment programmes by reducing over-prescribing of malaria treatments; and reduce the potential for the emergence of drug resistance as less individuals will have sub-therapeutic doses of treatment in their blood, therefore reducing selection pressure for resistant parasite strains (Whitty *et al.,* 2004). However, there are several obstacles to increasing diagnostic coverage in retail outlets. Testing may introduce an additional cost to treatment which patients may have been avoiding by accessing treatment from retail outlets, rather than health facilities. Tests require blood to be drawn which in outlets with poor health and safety practices may expose patients and staff to blood transmitted diseases such as Hepatitis B and HIV. Microscopes are expensive to purchase and maintain, and require training of staff for them to be used effectively. RDTs are easier to use to detect parasitaemia, however they are heat sensitive, which may be a concern in tropical countries.

Currently few data are available on the effects of introducing diagnostics to retail outlets. The limited evidence available suggests that this may not be straightforward, For example, a study in Western Kenya revealed that having subsidised RDTs in retail outlets did not change prescribing practices much with 60% of patients testing negative still being treated for malaria (Cohen, 2010). Similarly, the study in Cambodia described in Chapter 2, showed that even though subsidised RDTs were provided alongside subsidised ACTs, through the private sector, the availability and use of RDTs was still low (Sabot *et al.,* 2008). Although a number of other studies are underway in Uganda (FIND, 2011; Uganda NMCP, 2011), this area remains a topic of great debate and a research priority.

Finally it is important that the benefits and challenges of retail sector ACT provision are considered in comparison with other potential strategies to improved malaria treatment coverage, such as enhancing public sector provision or use of CHWs. In the public sector, widespread stockouts of essential drugs are a common occurrence, and represent one of the main causes of low public facility utilisation, reducing the quality of care received and increasing the economic burden on households who are forced to buy stocked out drugs from alternative private providers. Despite numerous attempts to strengthen public medicine supply, such as reforms to central medical stores and replacement of "push" systems with demand-based "pull" systems, these problems persist. A number of innovative initiatives are now being used to address this, including SMS based monitoring of drug supplies (SMS for Life, Tanzania) (Barrington *et al.,* 2010); hiring district level commodity planners (Zambia Access to ACT Initiative (The World Bank, 2010); allowing public facilities to purchase from private supplies (e.g. Tanzania, Niger); and the Stop Stock-outs Campaign (http://stopstockouts.org).

CHWs have been shown to provide high levels of ACT coverage, with a multicountry study in Ghana, Nigeria, and Uganda finding that 59% of children reporting fever in the past two weeks had received ACT from a CHW (Ajayi *et al.,* 2009). There is renewed interest in the potential for CHWs to deliver a range of Primary Health Care (PHC) interventions including malaria treatment (Nsabangani *et al.,* 2007, Tiono *et al.,* 2008, Ajayi *et al.,* 2008). In Kenya for example, there is talk of rolling out a "Community Strategy" based on CHW care, with the aim of using CHWs to supply malaria treatment within the AMF-m framework to communities in need (Ministry of Health Kenya, 2009). Additional advantages of using CHWs over retail providers include possible greater ease in introducing RDTs alongside ACTs, and the potential to provide care for other causes of fever at the same time Mukanga *et al.,*(2011). The WHO has been moving away from home management of malaria towards a strategy of integrated community case management (iCCM). ICCM provides a more holistic approach encompassing not only the treatment of malaria, but also pneumonia and diarrhoea which are the other major causes of morbidity and mortality in children under five. In this strategy, front line workers such as CHWs are equipped with the knowledge and supplies required to diagnose and treat these conditions. Studies carried out on iCCM have shown that it has the potential to improve treatment coverage and quality of care (World Malaria Report, 2011). However, there have been previous concerns raised regarding CHW's poor retention, the need to provide them with incentives, motivation and supervision (HENNET, 2007). More evidence is required to compare the costs and benefits of different HMM strategies at scale.

8.5: CONCLUSION

This study has demonstrated that an HMM intervention involving the provision of pre-packaged, subsidized AL delivered through the private retail sector accompanied by a one day training of providers and community awareness activities can significantly improve coverage of prompt effective anti-malarial treatment. The intervention was also successful in distributing the treatment equitably, reaching those poorest in the community who are in most need of the intervention. However, the intervention was less successful in improving adhering and dispensing practices.

Outstanding questions that require further research include an assessment of how such an intervention will perform at a larger scale and in other parts of the country, given the regional variation in epidemiology, health facilities, retail sector activity and socio-economic status. Further investigation is also needed on strategies to improve provider knowledge and application of this knowledge. There is also potential to introduce rapid diagnostic tests in retail outlets, as has been done nationwide in Cambodia (Sabot *et al.,* 2009), and piloted in Western Kenya (Cohen, 2010). Further investigation is clearly needed on whether and how this can be operationalized in Kenya. Further work is also needed on designing an effective system to monitor pharmacovigilance when ACTs are distributed more widely outside formal facilities. Finally, I did not conduct a cost-effectiveness analysis as part of this evaluation because the small scale clustered design meant that costs were unlikely to be representative of standard implementation. However, as such interventions are scaled up, it is important that such cost and cost-effectiveness studies are conducted to compare the value for money and affordability of ACT subsidy interventions with other approaches for improving malaria treatment using the public sector and community based strategies.

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APPENDICIES

APPENDIX I

SAMPLING PROCEDURES

Steps in selection of study sub-locations

- Sub-locations were allocated random numbers which were then sorted in ascending order.
- The sub-location at the top of the list was entered into the study as an intervention site, and removed from the sampling frame.
- Sub-locations on the list that were within two sub-locations of the selected sub-location were removed from the sampling frame. These sub-locations created the buffer to minimize possible contamination between study sites.
- Sub-locations within the new sampling frame were re-assigned random numbers and sorted in ascending order. This time the sub-location at the top of the list was entered into the control arm and removed from the list.
- All sub-locations on the list that were within two sub-locations of the selected control sub-location were then removed from the list .
- This process continued, alternating between intervention and control arm allocation until 3 intervention and 3 control sub-locations had been selected within each district. Teso and Busia districts neighbour each other, it was therefore important that any sub-locations selected near the border of these two districts were at least two sub-locations away from each other, regardless of the district borders. Sub-locations selected that were near to each other across borders had to be replaced by another selected through the same randomisation process.

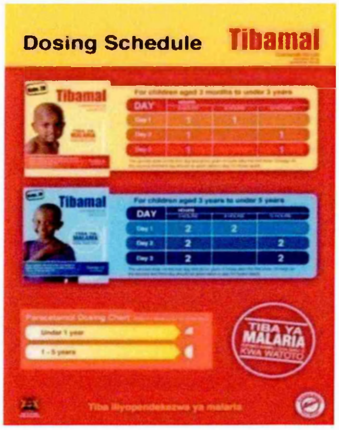
Steps in selection of Enumeration areas

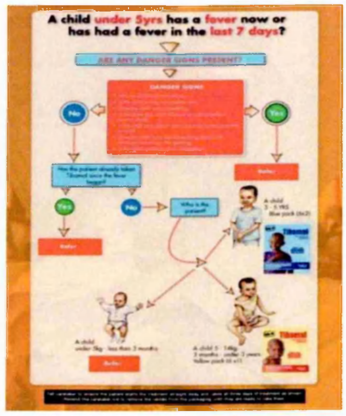
- A list of all EAs in the selected sub-districts was made with their total populations.
- Running cumulative population totals were calculated, together with a total population.
- The total population was divided by 3, the number of EAs I wish to select within a sub-location, the output of which was called the *sampling interval* (SI).
- A random number was chosen between 1 and the SI, this was called the *Random Start (RS)*.
- The first EA selected was the one in which the RS fell within its cumulative population i.e. between the cumulative number that proceeded the previous EA on the list and the cumulative total assigned to that EA.
- The RS was then added to the SI to calculate the 2nd RS, which was used to identify the 2nd EA, as described above.
- The 3rd RS was calculated as RS + 2SI, which was used to identify the 3rd EA.

APPENDIX 2

COMMUNITY AWARENESS MATERIALS

Dispensing Aids and Promotional Items for the Intervention





Tibamal® work aids used by retailers

An example of the Tibamal® wall painting

Tibamal® promotional T-shirt

Tibamal® Calendar

Pen

Tibamal® promotional pen

Tibamal® poster

APPENDIX 3

KEY INDICATORS FOR ACT ACCESS STUDIES IN KENYA

Background

Kenya has been delivering artemisinin combination therapy (ACT) through the public sector since mid-2006. Early evaluations show this led to an increase in the percentage of children under 5 receiving antimalarials from 14% to 26% within 48 hours, of whom 30% received artemether-lumefantrine (AL). However, access remains well below the Roll Back Malaria target of 60%, with the majority of patients still failing to receive prompt effective treatment. The Ministry of Health (MOH) is committed to exploring alternative delivery channels that can complement existing facility-level delivery, and thus improve community access to ACT. These could include delivery through drug retailers, Sustainable Health Enterprise Foundation (SHEF) clinics, Community Owned Resource Persons (CORPs) or other volunteers. Pilots of such interventions have been proposed by a number of groups, and the Pharmacy and Poisons Board (PPB) is expected to approve a special dispensation to allow over the counter (OTC) status for AL for these pilots.

The Division of Malaria Control (DOMC) is keen to ensure that evidence arising from these pilots is of high quality and based on common indicators, to facilitate comparison of results and identification of policy implications. This paper therefore outlines core indicators which should be included in all studies, and identifies optional complementary indicators which may also be included. In addition, each pilot may wish to add their own indicators that address outcomes specific to their interventions or interests. The indicators have been identified through consideration of DOMC targets, Global Fund (GF) and Roll Back Malaria Monitoring and Evaluation Reference Group (RBM MERG M&E) frameworks, and the draft monitoring and evaluation (M&E) guidelines for the global ACT subsidy.

Guidelines on Study Design

All studies must include either:

- Pre and post-intervention data
- Intervention and control groups

It is strongly recommended that both are included (i.e. pre and post for intervention and control groups). However, this may be infeasible for some studies, for example where the intervention has already begun, or where no appropriate control groups exist.

Cluster randomisation of outlets to intervention and control groups reduces the potential for bias. However, it may be infeasible for some interventions which need to function at a certain minimum scale, or where "contamination" would be likely between clusters (e.g. residents from control clusters could visit outlets in intervention clusters or receive communication messages targeted at the intervention group). In most cases it is therefore likely that there may be only 1 or 2 control and intervention areas.

Study Indicators

Indicators have been divided into 3 groups:

A. **Indicators to be included in all studies (please refer to back page for summary)**
B. **Optional complementary indicators**
C. **Indicators likely to be beyond the scope of pilot studies**

A. Indicators to be Included in all Studies
A1: Household Survey Indicators

Indicator 1: The proportion of children under 5 years with fever in the past 2 weeks who started treatment with a first line ACT within 24 and 48 hours of fever onset, overall, by socio-economic group (SEG) and treatment source

- This will be the primary indicator for all studies. It is a standard RBM indicator collected as part of the Multiple Indicator Custer Surveys (MICS) and the Demographic and Health Surveys (DHS) and a core GF indicator.
- It requires collection through a household survey, which will represent an additional expense for some pilots. However, it is essential in order to measure the overall impact on ACT coverage from both facility and non-facility sources. This is important as an intervention with high levels of ACT provision through non-facility sources would not be considered a success if it reduced facility provision, and possibly even reduced ACT coverage overall.
- All compulsory household survey indicators focus on children under 5 years as the most biologically vulnerable group. Older groups are also important, but their inclusion would increase the complexity of the household survey. The same indicators for these groups are therefore considered optional.
- 2 weeks is the standard recall period for this indicator.
- I focus on fever (rather than malaria) as the majority of febrile illnesses do not receive parasitological confirmation, and fever is the main symptom used in clinical diagnosis. In addition, for most communities in Africa, fever is the prompt for seeking treatment.
- I have included both 24 and 48 hours (although RBM targets have been specified in terms of 24 hours), as treatment within 48 hours could still be considered prompt. The denominator for 24 (48) hours should be all individuals reporting fever, visited 2 (3) or more days after symptoms began. Surveys must therefore also ask when symptoms began.
- The indicator should be collected by SEG in view of the emphasis placed on equity by both the Kenyan MOH, and RBM. All surveys should therefore include the standard asset indicators from the Kenya (K)DHS (collection of asset indicators is much quicker and more reliable than collection of income or expenditure data). Households should then be allocated to national SEGs on the basis of national KDHS weights. This is preferable to calculating a study specific asset index and SEGs, as, for example, households in socio-economic quintile 3 in one study area could be in quintile 5 in another.
- The indicator should be collected by treatment source (e.g. public, faith-based organisations (FBOs) and commercial facilities, pharmacies, other retail outlets and CORPs) in order to know through which channels the intervention is achieving its goals.

- Study teams should choose a sample size capable of detecting at least a 20 percentage point increase in ACT coverage in the target group (5% significance, 80% power, allowing for clustering if such sampling is used). As a rough guide, assuming an initial proportion of 11% (KEMRI/Wellcome Trust, 2007), with a simple random sample of households this would require a minimum of 65 childhood fevers per group (before and after, or control and intervention). In areas with moderate to high malaria transmission you are likely to need to visit between 2 and 4 households to find one childhood fever, meaning that you should sample at least 260 households in each group. If a cluster design is used it would be conservative to double this requirement to 520 households per group.
- It is recommended that tools such as picture boards are used to facilitate recall of drugs used.

Indicator 2: The proportion of children under 5 years with fever taking a first line ACT who adhered to the treatment dose, by source

- Adherence is important in both treatment efficacy and reducing the risk of the development of resistance.
- As ACT is a 3 day course, the denominator should be individuals interviewed 3 or more days after ACT treatment began.
- The indicator should be measured by source to indicate any variations in adherence across treatment types.
- Adherence will be defined as taking the quantity of drug specified in MOH guidelines by age group over 3 days (i.e. excludes both under and over dosing).
- Timing of doses within the 3 days will not be considered due to problems of precise time recall.

Indicator 3: The proportion of children under 5 years with fever who took an anti-malarial monotherapy in the past 2 weeks

- This assesses whether the intervention has succeeded in crowding monotherapies from the market, which are undesirable because they create competition that may decrease the demand for more effective combination therapies such as ACTs. The availability of artemisinin monotherapies increases the likelihood of the development of resistance to artemisinin, thus reducing the useful therapeutic life (UTL) of the ACTs.

Indicator 4: The proportion of children under 5 years with fever in the past 2 weeks who sought treatment by source (e.g. from public, mission & commercial health facilities, pharmacies, other retail outlets, CORPs, traditional healers and other sources)

- This indicator will allow assessment of any changes in treatment seeking patterns as a result of the intervention, for example whether there is a shift away from facilities, or from shops to CORPs, or an overall increase in the proportion seeking any care.
- The indicator covers any use of each outlet type, irrespective of the order in which they were used. One child may therefore use more than one source.

A2: Provider Survey Indicators

Indicator 5: The median price charged by non-facility outlets for a first line ACT by age band

- The price charged is important in order to assess affordability and whether subsidies are being passed onto final users i.e. are providers adhering to recommended retail prices or to free provision depending on the intervention design.
- I propose collecting drug price data from the provider survey rather than the household survey because of the difficulties of recall of costs in household surveys, the problems of separating the cost of a single drug from other payments, and problems of standardisation due to variation in patient age and dose obtained. It is possible that providers may not admit diverging from recommended prices under direct questioning, so an optional alternative is to validate price data through the patient- provider encounter indicators – see below.
- The median rather than the mean is generally used for cost and price data as the data tend to be skewed.

Indicator 6: The proportion of non-facility outlets with no expired first line ACT available in stock
Indicator 7: The proportion of non-facility outlets reporting stock outs of the first line ACT within the past 2 weeks

- A stock out is regarded as any period of time the facility does not contain stock. Restricting stock outs to a minimum period of time may complicate data collection in addition, an efficient supply chain should ensure that drugs are always available for customers to purchase.

Indicator 8: The proportion of non-facility outlets storing first line ACT appropriately

- Storage conditions include: (1) Off floor, (2) Out of direct sunlight, (3) Dry area, (4) Away from foodstuff, (5) All conditions met. "Appropriate storage" is defined as item (5) i.e. all storage conditions (1-4) have been met.

Indicator 9: The proportion of non-facility outlets that have copies of the materials/ job aids required by the intervention (e.g. leaflets, posters, guidelines)

A3: Intervention Cost Indicators

Ideally one would want cost data from all pilots in order to compare:

Indicator 10: Implementation cost per intervention area

- The cost of the intervention will provide information on the size of budget required to roll out a similar intervention either at a regional or national level.
- Costs should take into account all items that were paid for during the planning and rollout of the intervention. These include for example, costs of purchasing the anti-malarial drugs, costs of transport of staff and goods to and from intervention sites, salaries paid to all staff who played a part in planning and implementation of the intervention, and costs incurred from the development of information, education and communication materials.

Indicator 11: The cost-effectiveness in terms of the incremental cost per additional child receiving prompt ACT treatment

However, there are a number of challenges:

- Pilots tend to operate on a small scale and therefore costs may not be representative of larger scale operations, when costs per capita may fall significantly.
- Considerable effort is required to ensure that cost data collected are comparable.
- Cost data collection and analysis requires specific skills that may not be available to all partners.

A costing consultant will therefore be hired by the MOH to work with each team to estimate costs for scaled up operation of each pilot. This will facilitate the use of standardised methods and unit costs where appropriate, and avoid basing policy decisions on unrepresentative costs from differing small scale operations. It is therefore compulsory for all pilots to keep records of resource use, and to collaborate with the MOH in any costing analysis required.

A4: Pharmacovigilance Indicators

Pilots will be required to collaborate with regulatory authorities (PPB, MOH) to ensure that any pharmacovigilance requirements are met within their intervention design.

B. Optional complementary indicators

B1: Household Survey Indicators

- *Indicators 1-4 could be adapted to consider Individuals of 5 years and over*
- *Indicator 1 could be adapted to consider all antimalarials, or all "effective" antimalarials*
- *The proportion of non-target household members receiving intervention ACT (e.g. adults receiving paediatric ACT if ACT is targeted at children only; pregnant women receiving ACT)*
- *Household cost of fever episode (for all completed episodes)*
- *The proportion of households within 30 minutes to 1 hour travel time from a first line ACT source*
- *The proportion of caregivers with knowledge of malaria symptoms, danger signs, ACT and correct ACT dose for 2 year old*

B2: Provider Survey Indicators

- *Total volume of ACT distributed per capita in public and private sectors*
- *The proportion of sub-locations with at least one ACT source*
- *Availability of public sector ACT in inappropriate outlets*
- *Availability of private sector intervention ACT in inappropriate outlets*
- *The proportion of non-facility outlets with first line ACT stock records that correspond with physical counts*

The above indicators require a detailed understanding of a variety of factors for all service providers in the locality including the numbers, nature and antimalarial stocks. This is unlikely to be feasible for all studies.

B3: Patient- Provider Encounters Indicators

In addition to the household and provider surveys, it is necessary to include some evaluation of patient-provider interaction to give better information on actual (rather than self-reported) provider behaviour. Patient-provider interaction can be assessed by a number of methods including the following:

- Direct observation requires data collectors to directly observe the behaviour of the provider for the purpose of describing over the counter prescribing and dispensing practices.
- Mystery shopper study, where data collectors pose as ordinary customers. It provides similar information to direct observation, except the observer does not have to stay at the site for a substantial period of time; the potential bias from observation is eliminated and the scenarios assessed can be standardised between outlets. This technique does however raise some ethical concerns because informed consent is not obtained from the medicine seller before the study is conducted.
- Exit interviews provide information to determine how well each patient/caregiver understood the instructions given by the provider and also can be used as a record of reported patient provider interactions.
- Vignette surveys. These are short hypothetical scenarios described to the interviewee with the intention of eliciting a response from them. For example 'what would you do if a care giver presented with a 2 year old child with fever?'. The response is used to portray perceptions, opinions, beliefs and attitudes of the interviewee. The responses however do not provide any information on the actions of the care giver if presented with a similar real life situation as beliefs do not always translate into action.
- Management information systems involve using retrospective data collected by the non-facility outlet to determine the prescribing and dispensing practices of the provider

Data will not be strictly comparable between the above methods. However, no single method is possible in all studies for practical reasons. For example, it would not be efficient to do an exit interview where there are only a few customers per day; neither is it possible to use mystery shoppers at a clinic. Each study should therefore include the method most suitable to them.

Indicators for the patient provider encounters include:

- *The proportion of non-facility outlet staff that dispense an appropriate first line ACT to patients presenting with fever*
- *The proportion of non-facility outlet staff that dispense the correct dose of first line ACT to patients presenting with fever*
- *The proportion of non-facility outlets that provide appropriate information to patients/ caregivers on how to give/ take the first line ACT*

- *The proportion of encounters where non-facility outlet staff asked one or more clinical questions to determine severity of malaria*
- *The proportion of non facility outlet staff who told patients/ caregivers about any signs of progressive illness and recommended a referral visit to a doctor or clinic if the signs appear*
- *The median price charged for an ACT dose by age group*

B4: Qualitative Data Indicators

It is also recommended that studies include qualitative data collection activities such as focus group discussions and in-depth interviews with household members, providers and others involved in the distribution chain. These will complement, validate and help interpret the quantitative indicators, providing a richer understanding of the reasons behind achievements and constraints in implementation. Qualitative data may also be used to inform the design of quantitative instruments.

B5: Diagnostic Indicators

Diagnosis can be either clinical (presumptive) or parasitologically confirmed (microscopy or rapid diagnostic tests). It is likely that a mix of diagnostic approaches will be used across the studies. Where parasitologically confirmed diagnosis is used in an intervention, the following indicators should be evaluated:

- *The proportion of non-facility outlets staff able to confirm a malaria diagnosis according to national guidelines using the approved diagnostic*
- *The proportion of non-facility outlet patients who undergo a malaria diagnostic test*
- *The sensitivity and specificity of a diagnostic test*. Diagnostics should be of high sensitivity since false negatives may result in failure to treat, and of high specificity to avoid over diagnosis and subsequent over treatment.
- *The proportion of non facility outlets reporting stock outs of the approved diagnostic or components required for its proper functioning, within the past 2 weeks*

C. Indicators Likely to be Beyond the Scope of Pilot Studies

C1: Morbidity and Mortality Indicators

Final health outcome measures such as number of severe malaria cases and number of malaria fatalities would clearly be desirable. However, they are difficult to obtain for 2 reasons:

- They are relatively rare events and therefore require very large sample sizes;
- Many severe cases and deaths are not seen at health facilities and therefore are difficult to identify; over 60% of deaths in Kenya and in the sub-region occur at home.

It is therefore not expected that most studies will include these indicators. Exceptions may be large scale studies which could consider facility reports of severe cases, or studies taking place within demographic surveillance areas where community-based malaria mortality rates can be assessed based on verbal autopsy.

C2: Drug Resistance Indicators

Pilots are unlikely to be able to measure the impact of their intervention on drug resistance directly through treatment failure rates or genetic resistance markers. Measuring such outcomes would require large sample sizes, long time frames, and considerably increase evaluation costs in terms of collection of blood samples and laboratory analysis.

C3: Drug Quality Indicators

All pilots will use ACT supplies from quality certified sources and will therefore not be at risk of poor quality from sub-standard or fraudulent manufacturing. However, it is possible that the storage and handling of ACT in the supply chain could negatively affect quality, and these intermediate outcomes are therefore included under the provider survey. Again, additional laboratory tests would be required to assess the impact of storage and handling on actual quality.

APPENDIX 4

PCA ANALYSIS

There are several ways to determine household wealth/ socio-economic status which include standard economic measurers of monetary information such as household income, consumption or expenditure measures, however a limitation in using these measures is the extensive data collection required which may be both time consuming and costly. As a result asset-based measures are increasingly being used to determine socio-economic status of households (Vyas & Kumaranayake (2006)). In this technique, data are collected on households asset ownership, and housing characteristics. Principal component analysis (PCA) is used to determine appropriate weights for the assets, and produce a range of critical points which allows households to be differentiated by varying socio-economic levels. Further details on the use of this technique can be found in Filmer & Pritchett (2001)).

The presence of certain household assets (selected on the basis of those included in the 2003 Kenyan Demographic and Health survey (CBS,2004)) was recorded to assess the wealth of the household. A wealth index was constructed by assigning weights to each asset using PCA with weights based on the first principal component only. Missing asset data was replaced with the mean value for that variable, the mean derived from other households within the same enumeration area (Vyas & Kumaranayake (2006)). Each household was then assigned to a specific wealth quintile, those falling into the first quintile being most poor and those in the fifth quintile being least poor. All interviewed households were included in the PCA, regardless of whether they contained children under five. The PCA was conducted separately for baseline and follow-up surveys.

Baseline

The survey included data on 65 asset indicators. At baseline two asset indicator variables, 'using bottled water' and 'having an unlisted 'other' type of floor' were dropped from the analysis because of zero variance. The first principal component explained 6% of the variability in the SES variables. Table A4.1 reports the baseline weights from the principal components analysis of the remaining 63 variables, with the greatest weight given to having a cement floor: 0.379, a television: 0.294, corrugated iron sheets for the roof: 0.277, owning a ventilated pit latrine: 0.245, and owning a phone: 0.233. It should be noted that cooking with electricity was attributed a negative weight from the PCA, implying that a household cooking with electricity will be ranked lower in terms of SES than a household that does not cook with electricity. An explanation for this may be that the PCA strongly correlated cooking with electricity with variables associated with a lower SES, such as dumping waste on the street or empty plot (Vyas & Kumaranayake (2006)). The difference that ownership of each asset made to the household's PCA score is also displayed on Table A4.1 and was calculated by dividing the weight of each variable by its standard deviation. The greatest impact on the PCA score was having a tiled roof at 2.69, followed by a fridge at 2.118 and a car at 1.911.

The difference observed in mean socio-economic scores between the 1st and 2nd quintile was 0.671, the 2nd and 3rd quintile, 0.643 and the 3rd and 4th quintile, 0.759. The difference in mean socio-economic scores remained relatively equal between these quintiles, suggesting a uniformly distributed SES. The relatively small differences seen between the mean SES scores in these quintiles indicates that wealth does not change much moving from households in a lower quintile to those in a higher quintile. A histogram (Figure A4.1) plotting the socio economic scores shows scores were heavily skewed to the left, which may indicate evidence of truncation. This tends to occur if there are not sufficient indicators to allow one to tell between the poor and the very poor and may also be a possible explanation for the relatively small difference seen in wealth between the lower quintiles.

A larger gap exists between the mean socio-economic scores of the 4th and 5th quintile of 2.880, suggesting those in the highest quintile are disproportionately wealthier than those in the lower quintiles.

Table A4.1: Baseline PCA outputs

Variable	Mean	Standard Deviation	Weight	Impact on PCA score
Tiled roof	0.001	0.03	0.081	2.69
Fridge	0.002	0.046	0.098	2.118
Car	0.009	0.095	0.182	1.911
Vinyl or asphalt strips floor	0	0.017	0.031	1.759
Rain water	0.002	0.039	0.063	1.608
Own a ventilated improved pit latrine	0.029	0.167	0.245	1.469
Cooking with gas	0.001	0.035	0.051	1.467
Solar power	0.024	0.152	0.218	1.43
Ceramic tiled floor	0.001	0.035	0.049	1.413
Carpet floor	0.002	0.043	0.059	1.386
Cooking with Kerosene/ Paraffin	0.001	0.025	0.031	1.24
Cement floor	0.106	0.308	0.379	1.231
Motorcycle	0.015	0.121	0.144	1.191
Electricity	0.004	0.06	0.07	1.155
Television	0.105	0.306	0.294	0.959
Cooking with charcoal from wood/ coal/ lignite	0.026	0.158	0.145	0.918
Infrequent collection of waste by government	0	0.017	0.015	0.837
Pays for private collection of waste	0.001	0.025	0.02	0.819
Water from closed borehole or well in compound/ plot	0.055	0.227	0.168	0.739
Pays no rent on house (squatting)	0.001	0.03	0.02	0.668
Share a ventilated improved pit latrine	0.027	0.162	0.105	0.643
Corrugated Iron sheets roof	0.479	0.5	0.277	0.553
Water piped into compound/ plot	0.007	0.083	0.046	0.545
Phone	0.366	0.482	0.233	0.483
Regular collection of waste by government	0.001	0.03	0.015	0.483
Pays no rent on house with consent of owner	0.009	0.092	0.038	0.41
Radio	0 .691	0.462	0.164	0.354
Waste disposed in other method	0.001	0.025	0.008	0.34
Water from open borehole or well in compound/ plot	0.05	0.217	0.072	0.333
Asbestos sheets roof	0.001	0.035	0.011	0.315
Bicycle	0.595	0.491	0.146	0.298
Parquet or Polished wood floor	0	0.017	0.005	0.292
Waste composted	0.53	0.499	0.122	0.245
Water from public tap	0.016	0.127	0.03	0.236
Wooden planks floor	0.007	0.085	0.02	0.229
Water piped into dwelling	0.005	0.07	0.015	0.214
Own land	0.863	0.344	0.055	0.161
Share flush toilet	0.008	0.087	0.007	0.083
Own a pit latrine	0.375	0.484	0.035	0.072
Other roof	0.001	0.035	0.001	0.02
Water from closed borehole or well in open public	0.234	0.423	-0.021	-0.049
Water from open borehole or well in open public	0.125	0.331	-0.018	-0.054
Number of residents per sleeping room	2.88	1.511	-0.097	-0.064
Owns a flush toilet	0.006	0.076	-0.005	-0.065
Tin can roof	0.004	0.063	-0.009	-0.142

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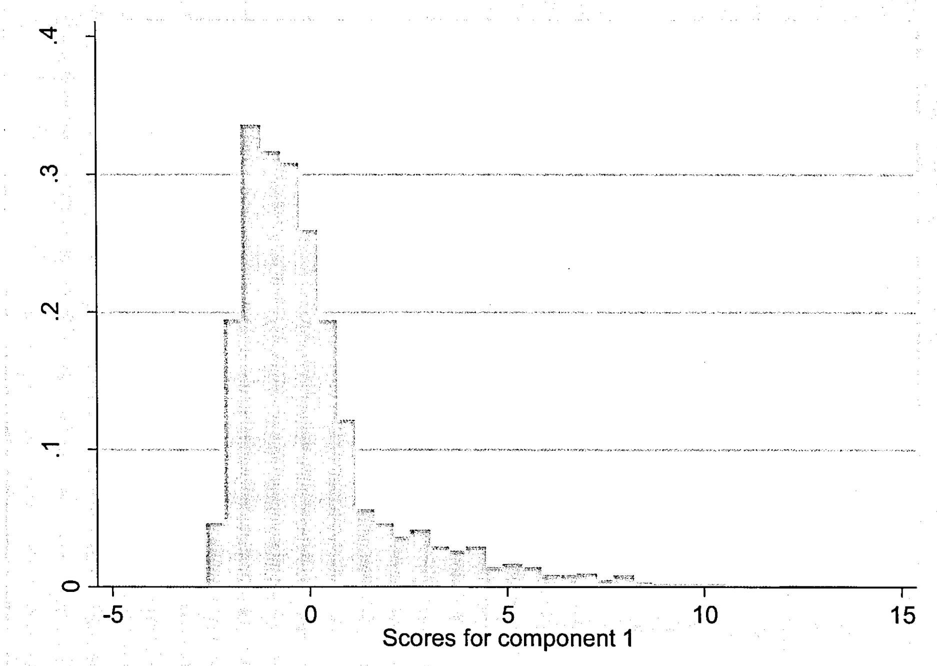
Table A4.1: Baseline PCA outputs continued

Variable	Mean	Standard Deviation	Weight	Impact on PCA score
Other toilet facility	0.004	0.063	-0.01	-0.156
Staying on land with owners consent	0.136	0.342	-0.053	-0.156
Waste dumped in street/ empty plot	0.108	0.311	-0.057	-0.184
Waste dumped, buried, burned in compound	0.359	0.48	-0.093	-0.193
Water from stream or river/ pond/ lake/ dam/ spring	0.5	0.5	-0.098	-0.195
Shares a pit latrine	0.481	0.5	-0.101	-0.202
Water from other source	0.007	0.085	-0.018	-0.214
Cooking with electricity	0.001	0.035	-0.009	-0.267
Renting house	0.001	0.025	-0.007	-0.276
Cooking with other fuel	0.001	0.03	-0.009	-0.291
Does not have a toilet [bush/ field]	0.071	0.257	-0.094	-0.364
Renting land	0.001	0.035	-0.013	-0.381
Own house	0.99	0.1	-0.039	-0.393
Concrete roof	0	0.017	-0.007	-0.395
Squatting on land	0.001	0.025	-0.011	-0.434
Grass or thatch/ Makuti roof	0.514	0.5	-0.281	-0.562
Cooking with Firewood/ Straw/ Dung	0.97	0.169	-0.147	-0.866
Earth/ sand/ mud/ dung floor	0.883	0.321	-0.384	-1.193

Figure A4.1: Histogram of baseline PCA scores



Follow-up

At follow-up 12 asset indicator variables were dropped from the analysis because of zero variance. These were owning floors made from: parquet or polished wood, vinyl or asphalt strips or any other type of floor not listed; owning a roof made from: tin cans, asbestos sheets or tiles; cooking with electricity, using bottled water, and having waste: collected on a regular or irregular basis by the government, by a private company or waste collected in any other way not listed. The first principal component explained 7% of the variability in the SES variables. Table A4.2 reports the follow-up weights from the principal components analysis of the remaining 53 variables, with the greatest weight given to having a cement floor: 0.375, having a corrugated iron sheet roof: 0.3, owning a television: 0.287, owning a ventilated pit latrine: 0.23, and owning a phone: 0.214. The difference that ownership of each asset made to the household PCA score is also displayed on Table A4.2 and is calculated by dividing the weight of each variable by its standard deviation. The greatest impact on the PCA score was having a concrete roof at 3.374, followed by a ceramic tiled floor at 2.75 and a fridge at 2.186.

Similar to baseline, the difference observed in mean socio-economic scores between the 1st and 2nd quintile was 0.761, the 2nd and 3rd quintile, 0.690 and the 3rd and 4th quintile, 0.784. The difference in mean socio-economic scores remained relatively equal between these quintiles, suggesting a uniformly distributed SES. The relatively small differences seen between the mean SES scores in these quintiles indicates that there the wealth does not change much moving from household in a lower to a higher quintile. As at baseline a histogram (Figure A4.2) plotting PCA scores showed evidence of truncation. A larger gap in the average index exists between the 4th and 5th quintile of 2.817, suggesting those in the highest quintile is disproportionately wealthier than those in the lower quintiles.

Table A4.2: Follow-up PCA outputs

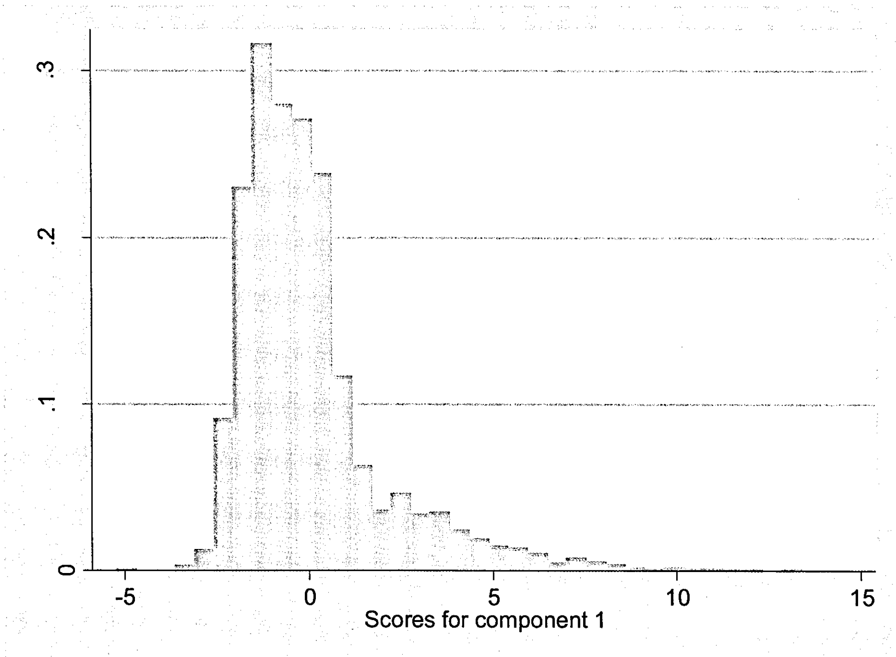
Variable	Mean	Standard Deviation	Weight	Impact on PCA score
Concrete roof	0	0.018	0.06	3.374
Ceramic tiled floor	0.001	0.025	0.069	2.75
Fridge	0.003	0.053	0.116	2.186
Cooking with Kerosene/ Paraffin	0	0.018	0.037	2.088
Electricity	0.003	0.056	0.113	2.019
Car	0.009	0.095	0.185	1.949
Owns a flush toilet	0.001	0.025	0.047	1.864
Carpet floor	0.001	0.025	0.046	1.84
Solar power	0.022	0.147	0.211	1.441
Own a ventilated improved pit latrine	0.026	0.16	0.23	1.432
Cooking with gas	0	0.018	0.025	1.422
Cement floor	0.114	0.318	0.375	1.18
Water from other source	0.001	0.031	0.035	1.15
Motorcycle	0.021	0.142	0.161	1.131
Water from stream or river/ pond/ lake/ dam/ spring	0.002	0.04	0.042	1.063
Piped into dwelling	0.002	0.043	0.046	1.051
Television	0.113	0.316	0.287	0.906
Cooking with charcoal from wood/ coal/ lignite	0.018	0.134	0.115	0.863
Share a ventilated improved pit latrine	0.019	0.136	0.116	0.856
Piped into compound/ plot	0.003	0.056	0.042	0.758
Corrugated Iron sheets roof	0.514	0.5	0.3	0.599
Closed borehole or well in compound/ plot	0.061	0.24	0.142	0.592
Phone	0.46	0.498	0.214	0.429
Radio	0.682	0.466	0.17	0.364
Bicycle	0.587	0.492	0.146	0.296
Own house	0.985	0.122	0.036	0.294
Wooden planks floor	0	0.018	0.005	0.293
Own land	0.902	0.297	0.087	0.292
Waste composted	0.424	0.494	0.135	0.273
Open borehole or well in compound/ plot	0.047	0.212	0.056	0.263
Cooking with other fuel	0.001	0.035	0.007	0.203
Owns a pit latrine	0.416	0.493	0.041	0.083

Table continued on next page

Table A4.2: Follow-up PCA outputs continued

Variable	Mean	Standard Deviation	Weight	Impact on PCA score
Renting land	0.001	0.025	0.001	0.024
Closed borehole or well in open public	0.265	0.441	-0.012	-0.027
Number of residents per sleeping room	2.752	1.425	-0.101	-0.071
Public tap	0.04	0.196	-0.022	-0.114
Open borehole or well in open public	0.156	0.363	-0.042	-0.115
Water from stream or river/ pond/ lake/ dam/ spring	0.423	0.494	-0.057	-0.115
Waste dumped, buried, burned in compound	0.473	0.499	-0.097	-0.194
Waste dumped in street/ empty plot	0.103	0.304	-0.06	-0.196
Other roof	0.001	0.035	-0.008	-0.215
Shares a pit latrine	0.471	0.499	-0.108	-0.216
Share flush toilet	0.001	0.035	-0.008	-0.22
Pays no rent on house with consent of owner	0.014	0.115	-0.029	-0.249
Staying on land with owners consent	0.097	0.296	-0.086	-0.29
Does not have a toilet [bush/ field]	0.064	0.245	-0.079	-0.321
Other toilet facility	0.001	0.035	-0.016	-0.457
Renting house	0.001	0.035	-0.018	-0.508
Grass or thatch/ Makuti roof	0.484	0.5	-0.301	-0.602
Cooking with Firewood/ Straw/ Dung	0.98	0.14	-0.12	-0.852
Earth/ sand/ mud/ dung floor	0.884	0.32	-0.382	-1.195
Other toilet facility	0	0.018	-0.024	-1.326
Squatting on land	0	0.018	-0.024	-1.326

Figure A4.2: Histogram of follow up PCA scores



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APPENDIX 5

PROVIDER SURVEY ANALYSIS BY OUTLET TYPE

INTRODUCTION

This appendix presents sub analyses carried out separately on specialized drug stores and retail outlets general stores, using what are considered to be the most important or informative indicators from Chapter 5 (Provider Survey Chapter) to assess whether the effects of the effects of the intervention were similar across outlet type. Due to the low numbers of outlets within each group, especially with specialized drug stores, and also minimising the negative effects of running multiple hypothesis tests this sub analyses can only be descriptive in nature

RESULTS

Table A5.1: Sample of outlets successfully interviewed, by type

	Baseline		Follow-up	
Number of outlets by type:	Control n (%)	Intervention n (%)	Control n (%)	Intervention n (%)
Specialised drug store	49/53 (92.5)	53/59 (89.8)	56/69 (81.2)	74/79 (93.7)
General store	214/242 (88.4)	152/165 (92.1)	262/299 (87.6)	246/272 (90.4)

Table A5.2: Educational background and age of staff who usually or occasionally serve customers- Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of outlets with at least one employee occasionally/ usually serving customers :	Control % (SD)	Intervention % (SD)
Any clinical related training[1]		
Baseline	67.4 (20.1)	59.3 (29.7)
Follow-up	78.8 (18.6)	72.6 (18.5)
Pharmacy/ pharmacy related training[2]		
Baseline	33.2 (23.4)	30.4 (18.4)
Follow-up	41.3 (14.6)	22.6 (22.8)
Nurse/ Nurse related training[3]		
Baseline	34.2 (20.7)	29.1 (19.7)
Follow-up	47.3 (28.5)	55.5 (19.6)
Medical doctor training[4]		
Baseline	1.6 (4.8)	8.6 (9.8)
Follow-up	3.2 (9.5)	3.3 (5.1)
Primary school incomplete or no education		
Baseline	12.5 (16.3)	12.1 (11.4)
Follow-up	0 (0)	6.1 (9.9)
Below 16 years of age		
Baseline	2.8 (8.3)	0 (0)
Follow-up	0 (0)	0 (0)

[1] Any clinical related training consists of: pharmacy, nurse and medical doctor related training; [2] Pharmacy related training includes pharmacy studied to a certificate or diploma level; [3]Nurse related training includes studying nursing to a certificate level (nurse aid) and diploma level; [4] Medical doctor training includes clinical officer who studied medicine to a diploma level

Table A5.3: Educational background and age of staff who usually or occasionally serve customers- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of outlets with at least one employee occasionally/ usually serving customers :	Control % (SD)	Intervention % (SD)
Any clinical related training[1]		
Baseline	10.1 (4.9)	9.1 (11.9)
Follow-up	1.8 (1.8)	2.7 (3.2)
Pharmacy/ pharmacy related training[2]		
Baseline	4.0 (5.8)	3.2 (5.1)
Follow-up	0 (0)	0.3 (1.0)
Nurse/ Nurse related training[3]		
Baseline	6.1 (5.9)	4.7 (7.5)
Follow-up	1.8 (1.8)	2.7 (3.2)
Medical doctor training[4]		
Baseline	1.2 (2.7)	1.2 (2.3)
Follow-up	0 (0)	0 (0)
Primary school incomplete or no education		
Baseline	30.0 (12.1)	33.1 (18.7)
Follow-up	28.1 (12.2)	34.7 (12.8)
Below 16 years of age		
Baseline	3.5 (7.0)	4.0 (4.1)
Follow-up	4.0 (4.0)	2.8 (3.5)

[1] Any clinical related training consists of: pharmacy, nurse and medical doctor related training; [2] Pharmacy related training includes pharmacy studied to a certificate or diploma level; [3]Nurse related training includes studying nursing to a certificate level (nurse aid) and diploma level; [4] Medical doctor training includes clinical officer who studied medicine to a diploma level

Table A5.4: Percentage of outlets that had at least one Tibamal® trained (mean of cluster summaries from the 9 intervention and 9 control clusters)

Tibamal® training:	Control % (SD)	Intervention % (SD)	Difference in means (95%CI)
Specialised drug stores	0 (0)	56.3 (14.3)	56.3 (46.2, 66.4)
General stores	1.1 (2.3)	38.4 (13.8)	37.2 (27.4, 47.1)

Table A5.5: Availability of AL in retail outlets- Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

AL availability:	Control % (SD) n	Intervention % (SD) n	Difference in means (95%CI)
Percentage of retail outlets with AL (including Tibamal®) in stock			
Baseline	3.8 (7.7) 2	5.4 (15.2) 2	
Follow-up	32.4 (21.7) 19	60.1 (26.7) 47	27.8 (3.4, 52.1)
Percentage of retail outlets with unexpired AL (including Tibamal®) in stock			
Baseline	3.8 (7.7) 2	3.6 (10.1) 2	
Follow-up	26.8 (23.0) 18	57.4 (31.7) 46	30.5 (2.9, 58.2)
Percentage of retail outlets with unexpired Tibamal® in stock			
Follow-up	0 (0) 0	48.5 (25.7) 40	48.5 (30.3, 66.6)
Percentage of outlets claiming to usually stock Tibamal® at follow-up[2]			
Follow-up	2.2 (6.7) 1	63.1 (25.6) 51	60.9 (42.2, 79.6)

Table A5.6: Availability of AL in retail outlets- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

AL availability:	Control (N=9) % (SD) n	Intervention (N=9) % (SD) n	Difference in means (95%CI)
Percentage of retail outlets with AL (including Tibamal®) in stock			
Baseline	0 (0)	1.2 (2.5) 2	
Follow-up	0 (0)	30.0 (11.4) 72	30.0 (21.9, 38.0)
Percentage of retail outlets with unexpired AL (including Tibamal®) in stock			
Baseline	0 (0)	0.7 (2.2) 1	
Follow-up	0 (0)	29.5 (11.7) 71	29.5 (21.2, 37.8)
Percentage of retail outlets with unexpired Tibamal® in stock			
Follow-up	0 (0)	29.5 (11.7) 71	29.5 (21.2, 37.8)
Percentage of outlets claiming to usually stock Tibamal® at follow-up[2]			
Follow-up	0 (0)	36.6 (12.2) 88	36.6 (28.0, 45.2)

Table A5.7: AL storage and stock outs at follow-up -Specialised drug store (mean of cluster summaries)

AL storage and stock outs:	Control (N=8) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Percentage of retail outlets storing all packs of AL appropriately	78.8 (24.7)	70.7 (33.7)	-8.0 (-39.0, 22.9)
Percentage of retail outlets with AL available, reporting stock outs of any of the AL packs within the past 2 weeks	6.3 (17.7)	39.9 (28.5)	33.7 (8.7, 58.6)

Table A5.8: AL storage and stock outs at follow-up -General stores (mean of cluster summary from the 9 intervention clusters)

AL storage and stock outs:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Percentage of retail outlets storing all packs of AL appropriately	-	85.9 (17.5)	-
Percentage of retail outlets with AL available, reporting stock outs of any of the AL packs within the past 2 weeks	-	25.5 (17.0)	-

Table A5.9: Median stock out days and tablet price of AL- Specialised drug stores (cluster summaries from the 9 intervention and 9 control clusters)

AL median stock out days and retail price at follow-up:	Control (N=9) Median (25%, 75% IQR)	Intervention (N=9) Median (25%, 75% IQR)
Median stock out days in outlets where AL was available (per AL available)	3 (3, 3)	5.4 (3.4, 9)
Retail price per AL tablet -KSH (including Tibamal®)		
Baseline	14.6 (4.2, 25)	19.4 (19.4, 19.4)
Follow-up	11.25 (6.32, 12.50)	3.33 (2.50, 3.33)

Table A5.10: Median stock out days and tablet price of AL- General stores (cluster summaries from the 9 intervention and 9 control clusters)

AL median stock out days and retail price at follow-up:	Control (N=9) Median (25%, 75% IQR)	Intervention (N=9) Median (25%, 75% IQR)
Median stock out days in outlets where AL was available (per AL available)	-	3.6 (2.8, 6.8)
Retail price per AL tablet -KSH (including Tibamal®)		
Baseline		
Follow-up	-	1.67 (1.67, 3.33)

Table A5.11: The percentage of outlets found with one or more anitmalarials in stock (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
Percentage of **specialised drug store** with AM in stock:			
Baseline	97.8 (6. 7)	97.2 (5.5)	
Follow-up	88.6 (18.9)	89.8 (11.2)	1.2 (-14.3, 16.7)
Percentage of **general store** with AM in stock:			
Baseline	41.8 (12.5)	52.1 (12.7)	
Follow-up	29.2 (11.2)	45.6 (7.9)	16.4 (6.7, 26.0)

Table A5.12: Antimalarials available, per retail outlet- Specialised drug stores (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of specialised drug store with certain AM in stock:	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
Amodiaquine:			
Baseline	96.4 (7.4)	94.0 (8.2)	
Follow-up	37.3 (31.2)	28.9 (16.4)	-8.4 (-33.4, 16.5)
Sulphadoxine-pyrimethamine:			
Baseline	83.0 (25.4)	78.5 (19.8)	
Follow-up	51.9 (25.1)	67.4 (12.4)	15.5 (-4.2, 35.3)
Quinine:			
Baseline	47.3 (27.3)	46.1 (13.6)	
Follow-up	59.6 (16.5)	48.9 (19.3)	-10.7 (28.6, 7.3)
Chloroquine:			
Baseline	5.0 (10.0)	5.4 (15.2)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Artemisinin monotherapy:			
Baseline	27.2 (27.5)	14.5 (15.7)	
Follow-up	17.4 (17.3)	4.4 (5.4)	-13.0 (-25.8, -0.2)
AL (including Tibamal®):			
Baseline	3.8 (7.7)	5.4 (15.2)	
Follow-up	32.4 (32.4)	60.1 (26.7)	27.8 (3.4, 52.1)
Tibamal®:			
Baseline	-	-	
Follow-up	0 (0)	48.5(25.7)	48.5 (30.3, 66.6)
ACT:			
Baseline	3.5 (7.2)	0 (0)	
Follow-up	9.8 (12.5)	0 (0)	-9.8 (-18.6, -1.0)

Table A5.13: Antimalarials available, per retail outlet- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of general stores with certain AM in stock:	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
Amodiaquine:			
Baseline	38.5 (9.2)	43.6 (15.2)	
Follow-up	16.3 (7.4)	10.5 (5.2)	-5.8 (-12.2, 0.6)
Sulphadoxine-pyrimethamine:			
Baseline	14.7 (10.0)	20.9 (10.7)	
Follow-up	15.5 (12.4)	17.5 (9.4)	2.0 (-9.0, 13.0)
Quinine:			
Baseline	2.1 (2.6)	0.5 (1.5)	
Follow-up	0.5 (1.4)	0 (0)	-0.5 (-1.5, 0.5)
Chloroquine:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Artemisinin monotherapy:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0.4 (1.3)	0.4 (-0.5, 1.3)
AL (including Tibamal®):			
Baseline	0 (0)	1.2 (2.5)	
Follow-up	0 (0)	30.0 (11.4)	30.0 (21.9, 38.0)
Tibamal®:			
Baseline	-	-	
Follow-up	0 (0)	30.0 (11.4)	30.0 (21.9, 38.0)
ACT:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0.4 (1.3)	0.4 (-0.5, 1.4)

Table A5.14: Providers' knowledge on symptoms of uncomplicated and uncomplicated malaria in a four year old child and symptoms of adverse drug reactions to AL (mean of cluster summaries from the 9 intervention and 9 control clusters)

Providers' knowledge on symptoms of uncomplicated malaria in a four year old child:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Specialised drug store:			
Baseline	100	92.0 (17.1)	
Follow-up	100	100	0 (100,100)
General store:			
Baseline	95.8 (3.0)	94.9 (4.7)	
Follow-up	96.2 (1.8)	99.3 (1.5)	3.0 (1.4, 4.7)
Providers' knowledge on symptoms of complicated malaria in a four year old child:			
Specialised drug store:			
Baseline	80.6 (18.3)	87.9 (14.8)	
Follow-up	84.3 (17.0)	89.5 (14.4)	5.2 (-10.5, 20.9)
General store:			
Baseline	71.7 (7.0)	77.0 (14.0)	
Follow-up	81.4 (10.1)	83.7 (11.4)	2.3 (-8.4, 13.0)
Percentage of respondents knowing AL ADR symptoms			
Specialised drug store:			
Baseline	53.4 (33.1)	53.9 (53.9)	
Follow-up	51.2 (15.5)	41.9 (25.0)	-9.4 (-30.1, 11.4)
General store:			
Baseline	18.0 (6.6)	11.8 (8.6)	
Follow-up	15.8 (13.3)	20.1 (20.2)	4.3 (-12.7, 21.4)

Table A5.15: Providers knowing the recommended treatment for uncomplicated malaria (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage knowing the first line AM for uncomplicated malaria:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Specialised drug store:			
Baseline	66.5 (28.2)	66.3 (18.6)	
Follow-up	81.0 (21.1)	83.9 (11.0)	2.9 (-14.0, 19.7)
General store:			
Baseline	31.2 (10.4)	22.9 (12.5)	
Follow-up	38.3 (14.4)	66.8 (12.0)	28.6 (-15.3, 41.8)

Table A5.16: Advice on where to first seek treatment for uncomplicated malaria in a four year old child- Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	19.8 (13.6)	21.1 (33.2)	
Follow-up	20.8 (18.8)	6.4 (10.2)	-14.4 (-29.5, 0.8)
Buy medication from a retail outlet :			
Baseline	74.7 (17.2)	76.3 (33.0)	
Follow-up	72.1 (23.6)	91.4(10.8)	19.3 (1.0, 37.6)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Would not know what to do:			
Baseline	0 (0)	0 (0)	
Follow-up	1.6 (4.8)	0 (0)	-1.6 (-5.0, 1.8)
Other[2]:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)

[1]P value refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. P value remains the same when adjusted for outlet type. [2] Other includes treatment at home with western medications, keeping the child warm when it is cold and maintaining good hygiene.

Table A5.17: Advice on where to first seek treatment for uncomplicated malaria in four year old child- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	43.1 (19.5)	45.6 (14.8)	
Follow-up	51.0 (13.6)	30.81 (11.9)	-20.2 (-7.4, -32.9)
Buy medication from a retail outlet:			
Baseline	47.7 (18.5)	47.5 (15.5)	
Follow-up	45.3(14.6)	64.3 (9.7)	19.0 (31.4, 6.6)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0(0)	0 (0,0)
Would not know what to do:			
Baseline	6.3 (2.3)	3.3 (3.2)	
Follow-up	2.5 (3.1)	1.5 (2.3)	-1.0 (-3.7, 1.8)
Other[2]:			
Baseline	0.8 (1.7)	0.4 (1.2)	
Follow-up	0 (0)	0.5 (1.4)	0.5 (-0.5, 1.4)

[1]P value refers to the level of significance of the unadjusted difference between control and intervention arms at follow-up. P value remains the same when adjusted for outlet type. [2] Other includes treatment at home with western medications, keeping the child warm when it is cold and maintaining good hygiene.

Table A5.18: Advice on where to first seek treatment for complicated malaria in a four year old-Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	60.3 (17.0)	64.9 (20.0.)	
Follow-up	79.5 (13.4)	72.9 (14.0)	-6.6 (-20.2, 7.1)
Buy medication from a retail outlet:			
Baseline	30.6 (17.4)	33.1 (17.8)	
Follow-up	20.8. (17.7)	23.0 (.13.1)	2.2 (-13.4, 17.8)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Would not know what to do:			
Baseline	0 (0)	0 (0)	
Follow-up	1.6 (4.8)	0 (0)	-1.6 (-5.0, 1.8)
Other[2]:			
Baseline	1.4 (4.2)	1.8 (5.1)	
Follow-up	1.6 (4.8)	3.3 (7.1)	1.7 (-4.3, 7.8)

[2]Other includes praying and sponging the child.

Table A5.19: Advice on where to first seek treatment for complicated malaria in a four year old-General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Advice on where to seek treatment:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Health facility:			
Baseline	75.4 (16.9)	80.3(10.9)	
Follow-up	84.8 (7.1)	90.4 (4.3)	5.6 (-0.2, 11.5)
Buy medication from a retail outlet:			
Baseline	14.0 (14.4)	14.4 (9.7)	
Follow-up	9.0 (4.9)	4.9 (4.8)	-1.6 (-6.5, 3.2)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Would not know what to do:			
Baseline	5.6(3.0)	3.1 (4.8)	
Follow-up	4.6 (3.7)	2.3 (2.8)	-2.3 (-5.6, 0.1)
Other[2]:			
Baseline	0.3 (0.9)	1.1 (3.3)	
Follow-up	1.4 (1.7)	0.6 (1.8)	-0.8 (-2.5, 0.9)

[2]Other includes praying and sponging the child.

Table A5.20: Respondents giving the correct dispensing advice for AL use in a four year old-Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of respondents that knew the correct AL advice:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
AL administration:			
Baseline	3.6 (7.4)	0 (0)	
Follow-up	2.2 (6.7)	25.6 (21.7)	23.4 (7.4, 39.5)
What to do if the child vomits AL:			
Baseline	0 (0)	0 (0)	
Follow-up	8.7 (13.8)	18.6 (14.1)	9.9 (4.0, 23.8)
What to do if the child does not improve:			
Baseline	70.9 (12.6)	70.4 (21.2)	
Follow-up	60.3 (23.2)	80.5 (18.6)	20.2 (-0.8, 41.2)
Foods to give the child with AL:			
Baseline	16.9 (19.3)	11.6 (11.4)	
Follow-up	5.7 (10.0)	40.9 (16.3)	35.1 (21.6, 48.6)

Table A5.21: Respondents giving the correct dispensing advice for AL use in a four year old- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Percentage of respondents that knew the correct AL advice:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
AL administration :			
Baseline	0 (0)	0 (0)	
Follow-up	1.1 (1.8)	9.5 (8.5)	8.4 (2.3, 14.6)
What to do if the child vomits AL:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	6.4 (6.4)	6.4 (1.9, 11.0)
What to do if the child does not improve:			
Baseline	40.0 (11.5)	40.3 (15.9)	
Follow-up	35.4 (.17.8)	60.6 (15.3)	25.1 (8.6, 41.7)
Foods to give the child with AL:			
Baseline	6.5 (6.5)	5.9 (5.9)	
Follow-up	6.0 (6.0)	22.8 (11.3)	16.8 (7.8, 25.8)

Table A5.22: Respondents' referral practices for suspected AL ADRs- Specialised drug store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Referral practices for suspected AL ADRs:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Percentage of outlets that would immediately refer patients to a health facility for a suspected ADR:			
Baseline	24.3 (18.3)	50.7 (20.9)	
Follow-up	30.6 (15.2)	39.2(23.1)	8.5 (-11.0, 28.0)
Percentage of outlets that had observed a suspected AL ADR:			
Baseline	32.8 (34.3)	24.7 (33.1)	
Follow-up	30.9 (25.8)	25.2 (13.4)	-5.7 (-26.2, 14.9)

Table A5.23: Respondents' referral practices for suspected AL ADRs- General store (mean of cluster summaries from the 9 intervention and 9 control clusters)

Referral practices for suspected AL ADRs:	Control (N=9) % (SD)	Intervention (N=9) % (SD)	Difference in means (95%CI)
Percentage of outlets that would immediately refer patients to a health facility for a suspected ADR:			
Baseline	27.0 (12.9)	21.9 (15.4)	
Follow-up	39.5 (10.9)	46.2 (13.6)	6.6 (-5.7, 19.0)
Percentage of outlets that had observed a suspected AL ADR:			
Baseline	8.8 (9.0)	11.4 (11.5)	
Follow-up	7.2 (8.3)	6.6 (6.9)	-0.6 (-8.3, 7.0)

Table A5.24: Respondents' use of CHW referral forms at follow-up (mean of cluster summaries from the 9 intervention and 9 control clusters)

CHW referral forms:	Control (N=9) % (SD)	Intervention (N=9) % (SD)
Percentage of outlets with CHW forms		
Specialised drug outlets:	1.9 (5.6)	56.1 (23.5)
General store:	2.0 (1.9)	32.7 (16.9)

APPENDIX 6

HOUSEHOLD SURVEY SUB-GROUP ANALYSIS

Table 7.4: Percentage of febrile children for whom care was obtained from general stores at baseline by characteristic of the child (mean of cluster summaries of the 9 intervention and 9 control clusters)

Children's characteristics:	Control (N=9) % (SD) n=41	Intervention (N=9) % (SD) n=55	Difference in means (95% CI)
Age:			
3 months to < 36 months	7.2 (4.7)	10.5 (5.1)	3.2 (8.2, -1.7)
36-59 months	10.9 (7.7)	16.7 (9.2)	5.8 (14.3, -2.7)
Sex:			
Male	7.8 (6.7)	12.5 (4.7)	4.7 (10.5, -1.1)
Female	8.6 (7.2)	12.9 (7.5)	4.3 (11.6, -3.1)
Household head's education			
Primary incomplete	7.3 (4.9)	13.6 (8.9)	6.3 (13.5, -0.8)
Primary complete and above	8.2 (7.1)	11.6 (6.7)	3.4 (10.3, -3.5)
ITN use:			
ITN use last night	1.7 (1.1)	3.0 (2.3)	1.2 (3.0, -0.6)
No ITN use last night	3.1 (3.4)	4.0 (1.8)	0.9 (3.6, -1.8)
Socio-economic status (wealth quintiles):			
Quintile 1 (most poor)	13.8 (12.3)	12.6 (15.3)	1.3 (12.6, -15.2)
Quintile 2 (very poor)	4.5 (7.7)	15.6 (14.3)	11.1 (22.6, -0.4)
Quintile 3 (poor)	2.2 (6.7)	9.6 (13.5)	7.4 (18.1, -3.2)
Quintile 4 (less poor)	7.0 (15.0)	12.0 (11.2)	5.0 (18.2, -8.2)
Quintile 5 (least poor)	15.5 (10.8)	4.8 (7.1)	-10.7 (-1.6, -20.0)

n= number of febrile children obtaining care from the general store

Table 7.4: Percentage of febrile children for whom care was obtained from general stores at follow up by characteristic of the child (mean of cluster summaries of the 9 intervention and 9 control clusters)

Children's characteristics:	Control (N=9) % (SD) n=67	Intervention (N=9) % (SD) n=113	Difference in means (95% CI)
Age:			
3 months to < 36 months	13.7 (6.4)	25.5 (25.5)	11.8 (2.7, 20.9)
36-59 months	31.9 (27.9)	24.5 (16.9)	-7.4 (15.7, -30.4)
Sex:			
Male	17.6 (9.4)	24.9 (12.9)	7.3 (18.5, -4.0)
Female	22.5 (13.3)	25.8 (15.0)	3.2 (17.4, -11.0)
Household head's education			
Primary incomplete	23.3 (17.2)	25.3 (11.3)	2.0 (16.5, -12.5)
Primary complete and above	14.8 (7.2)	25.1 (14.8)	10.3 (22.0, -1.3)
ITN use:			
ITN use last night	18.7 (11.4)	23.5 (15.2)	4.8 (18.3, -8.7)
No ITN use last night	20.6 (11.4)	25.9 (13.4)	5.3 (17.8, -7.2)
Socio-economic status (wealth quintiles):			
Quintile 1 (most poor)	20.5 (20.1)	25.4 (13.4)	4.9 (21.9, -12.2)
Quintile 2 (very poor)	17.0 (18.6)	22.5 (17.3)	5.5 (23.4, -12.5)
Quintile 3 (poor)	27.8 (15.3)	32.8 (19.6)	5.0 (22.6, -12.6)
Quintile 4 (less poor)	25.4 (31.5)	21.5 (23.2)	-3.8 (23.8, -31.5)
Quintile 5 (least poor)	25.6 (30.9)	12.9 (15.5)	-12.7 (11.7, -37.1)

n= number of febrile children obtaining care from the general store

Table 7.5: Percentage of febrile children for whom care was obtained from specialised drug stores at baseline by characteristic of the child (mean of cluster summaries of the 9 intervention and 9 control clusters)

Children's characteristics:	Control (N=9) % (SD) n=113	Intervention (N=9) % (SD) n=168	Difference in means (95% CI)
Age:			
3 months to < 36 months	29.0 (9.1)	35.6 (10.4)	6.6 (16.4, -3.2)
36-59 months	32.5 (12.1)	40.4 (16.1)	7.8 (22.1, -6.4)
Sex:			
Male	35.6 (12.4)	36.6 (13.0)	1.5 (13.8, -11.7)
Female	24.2 (8.4)	36.6 (18.2)	12.4 (26.6, -1.7)
Household head's education:			
Primary incomplete	29.0 (14.2)	31.2 (12.3)	2.1 (15.4, -11.1)
Primary complete and above	31.9 (9.4)	43.7 (11.6)	11.8 (22.4, 1.2)
ITN use:			
ITN use last night	7.8 (4.6)	13.1 (6.6)	5.3 (10.9, -0.4)
No ITN use last night	6.8 (2.7)	9.3 (5.3)	2.3 (6.7, -1.6)
Socio-economic status (wealth quintile):			
Quintile 1 (most poor)	34.1 (28.1)	33.4 (17.1)	0.7 (22.6, -23.9)
Quintile 2 (very poor)	34.3 (18.8)	30.7 (12.8)	3.7 (12.3, -19.8)
Quintile 3 (poor)	26.2 (30.0)	37.9 (18.5)	11.8 (32.6, -9.1)
Quintile 4 (less poor)	31.9 (17.8)	42.0 (27.4)	10.1 (33.2, -13.0)
Quintile 5 (least poor)	36.5 (25.8)	46.1 (33.5)	9.6 (39.4, -20.3)

n= number of febrile children obtaining care from the specialised drug store

Table 7.5: Percentage of febrile children for whom care was obtained from specialised drug stores at follow up by characteristic of the child (mean of cluster summaries of the 9 intervention and 9 control clusters)

Children's characteristics:	Control (N=9) % (SD) n=78	Intervention (N=9) % (SD) n=121	Difference in means (95% CI)
Age:			
3 months to < 36 months	25.7 (10.2)	25.4 (16.0)	-0.3 (13.1, -13.7)
36-59 months	13.8 (13.3)	35.3 (18.0)	21.5 (5.6, 37.3)
Sex:			
Male	24.8 (3.4)	30.2 (19.2)	5.4 (19.1, -8.4)
Female	19.5 (13.4)	27.3 (13.3)	7.9 (21.2, -5.5)
Household head's education:			
Primary incomplete	18.3 (5.2)	31.2 (19.1)	13.0 (27.0, -1.1)
Primary complete and above	27.4 (13.0)	26.4 (14.6)	-1.1 (12.8, -14.9)
ITN use:			
ITN use last night	22.4 (9.4)	28.9 (16.0)	6.5 (19.6, -6.7)
No ITN use last night	20.1 (12.3)	27.1 (15.9)	7.0 (21.2, -7.2)
Socio-economic status (wealth quintile):			
Quintile 1 (most poor)	20.5 (16.7)	28.1 (18.7)	7.6 (25.4, -10.1)
Quintile 2 (very poor)	28.5 (17.4)	28.2 (17.1)	-0.3 (17.0, -17.5)
Quintile 3 (poor)	15.8 (16.5)	22.6 (25.7)	6.8 (28.3, -14.8)
Quintile 4 (less poor)	31.3 (23.9)	31.0 (24.2)	-0.3 (23.7, -24.4)
Quintile 5 (least poor)	19.5 (21.1)	32.7 (11.9)	13.2 (30.3, -3.9)

n= number of febrile children obtaining care from the specialised drug store

APPENDIX 7

HOUSEHOLD SURVEY: FURTHER ANALYSIS ON TREATMENT SEEKING BEHAVIOUR

Table A7.1 shows a breakdown of actions taken by caregivers to treat their child suffering from a fever with two weeks prior to the interview. As a first action most care givers reported visiting either a government facility or a specialised drug store to obtain treatment. No significant differences were observed between actions in the control compared to the intervention arm. Similar patterns were observed in subsequent actions taken and very few caregivers reported taking more than three actions.

Table A7.1: Actions taken to treat children with fever in the last two weeks, by order of action (mean of cluster summaries from the 9 intervention and 9 control clusters)

Action number:	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
1st			
Government facility:			
Baseline	30.1 (11.3)	23.8 (11.7)	
Follow-up	33.6 (15.8)	26.4 (9.4)	-7.2 (5.8, -20.2)
Specialised drug store:			
Baseline	28.9 (14.9)	37.0 (16.2)	
Follow-up	22.7 (10.0)	28.9 (16.7)	6.2 (19.9, -7.5)
General store:			
Baseline	10.1 (4.5)	12.4 (4.7)	
Follow-up	19.7 (9.6)	25.6 (13.7)	5.9 (17.7, -5.9)
Missionary/Private facility:			
Baseline	5.8 (5.1)	6.3 (6.2)	
Follow-up	8.9 (5.3)	6.1 (8.1)	-2.8 (4.0, -9.6)
Traditional healer:			
Baseline	0.5 (1.4)	0 (0)	
Follow-up	0.4 (1.2)	0.6 (1.9)	0.2 (1.8, -1.3)
Others:			
Baseline	13.0 (6.0)	6.6 (6.2)	
Follow-up	8.6 (5.6)	5.7 (2.8)	-2.9 (1.5, -7.3)
2nd			
Government facility:			
Baseline	2.5 (2.8)	3.1(4.0)	
Follow-up	2.8 (3.0)	1.6 (1.4)	-1.1 (1.2, -3.5)
Specialised drug store:			
Baseline	5.1 (4.2)	4.6 (3.6)	
Follow-up	0.9 (1.7)	1.3 (1.6)	0.4 (2.1, -1.2)
General store:			
Baseline	0.8 (1.3)	1.0 (1.4)	
Follow-up	0.4 (1.2)	1.5 (2.1)	1.1 (2.9, -0.6)
Missionary/Private facility:			
Baseline	1.6 (1.9)	2.0 (1.8)	
Follow-up	0.4 (1.3)	0 (0)	-0.4 (0.5, -1.4)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0.3 (0.8)	0 (0)	-0.3 (0.3, -0.8)
Others:			
Baseline	1.1 (1.8)	1.5 (1.9)	
Follow-up	0.6 (1.3)	1.4 (2.0)	0.7 (2.4, -1.0)

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Table A7.1 continued

3rd			
Government facility:			
Baseline	0 (0)	0.5 (0.8)	
Follow-up	0 (0)	0.2 (0.6)	0.2 (0.7, -0.2)
Specialised drug store:			
Baseline	0.2 (0.5)	0.4 (1.1)	
Follow-up	0.3 (0.8)	0.2 (0.6)	-0.1 (0.6, -0.7)
General store:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Missionary/Private facility:			
Baseline	0 (0)	0.4 (1.2)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Others:			
Baseline	0.3 (0.8)	0.2 (0.6)	
Follow-up	0.2 (0.7)	0 (0)	0.2 (-0.3, 0.8)
4th			
Government facility:			
Baseline	0 (0)	0.2 (0.6)	
Follow-up	0 (0)	0.2 (0.6)	0.2 (0.6, -0.2)
Specialised drug store:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
General store:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Missionary/Private facility:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Traditional healer:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)
Others:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0, 0)

Other includes treatment at home with home-made remedies or western medication, traditional healers or prayers.

Types of AM prescribed by source

Table A7.2 shows the percentage of antimalarial monotherapies dispensed over the total number of visits made to each source of care. Amodiaquine was the most common monotherapy to be received, mostly from specialised drug stores followed by general stores. Overall there was a decline in amodiaquine dispensing from baseline to follow-up. There was a significant difference in amodiaquine dispensed from general stores between the arms with a decline to 3.1% (SD: 5.7%) of caregivers reporting to receive it in the intervention arm and 23.5% (15.5%) in the control arm. By the time of the study, amodiaquine was no longer being supplied to government hospitals, so it is surprising to see caregivers reporting to have received amodiaquine from this source. There are several potential explanations for this, including the possibility that some facilities had stock remaining after supply was discontinued, and may have used this when the first line therapy was out of stock

Quinine was the second most common monotherapy dispensed. At the time of study, quinine was Kenya's second line therapy for uncomplicated malaria and also used as first line treatment in complicated malaria (DOMC, 2007). Quinine was most commonly dispensed from mission and private hospitals, as well as government facilities. No significant difference was observed in the dispensing of quinine from baseline to follow-up. Few caregivers reported receiving SP, with the majority having received it from mission or private facilities. Both chloroquine and artemisinin monotherapies were reported to have been received by very few caregivers. One caregiver visit to a government facility in the control arm (0.4% (SD:1.3%) and one in the intervention arm 0.8% (SD:2.4%), were reported to have resulted in chloroquine being dispensed, however the supply of chloroquine to government facilities was discontinued many years ago and it is very likely that the caregivers may have misidentified the monotherapy they received.

Table A7.2: Types of antimalarial monotherapy prescribed by number of visits to source (mean of cluster summaries from the 9 intervention and 9 control clusters)

Antimalarial monotherapy source:	Control % (SD)	Intervention % (SD)	Difference in means (95% CI)
Amodiaquine:			
Specialised drug store:			
Baseline	44.5 (16.2)	43.9 (14.1)	
Follow-up	20.3 (19.9)	6.4 (6.4)	13.9 (-1.1, 28.9)
Mission_Private:			
Baseline	16.0 (26.9)	18.9 (.14.5)	
Follow-up	6.3 (13.8)	7.4 (22.2)	-1.1 (-19.6, 17.4)
Government facility:			
Baseline	20.8 (14.5)	18.1 (15.6)	
Follow-up	4.7 (5.6)	6.2 (6.9)	-1.5 (-7.8, 4.8)
General stores:			
Baseline	23.5 (20.7)	18.7 (17.8)	
Follow-up	23.5 (15.5)	3.1 (5.7)	20.4 (8.7, 32.1)
Other sources:			
Baseline	14.6 (11.8)	9.2 (11.3)	
Follow-up	4.4 (13.3)	3.7 (11.1)	0.7 (-11.5,13.0)
Sulphadoxine-pyrimethamine			
Specialised drug store:			
Baseline	1.8 (4.0)	9.0 (3.9)	
Follow-up	6.0 (7.7)	3.8 (7.3)	2.2 (-5.3, 9.7)
Mission_Private:			
Baseline	12.5 (35.4)	4.4(9.1)	
Follow-up	13.3 (33.2)	0 (0)	13.3 (-10.1, 36.8)
Government facility:			
Baseline	0.9 (1.8)	1.9 (2.6)	
Follow-up	3.7 (11.1)	0 (0)	3.7 (-4.1, 11.6)
General stores:			
Baseline	8.5 (13.4)	6.5 (9.8)	
Follow-up	2.5 (5.2)	3.1 (6.6)	-0.6 (-6.6, 5.3)
Other sources:			
Baseline	1.2 (3.7)	5.8 (9.0)	
Follow-up	4.4 (13.3)	3.7 (11.1)	0.7 (-11.5, 13.0)

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Table A7.2 continued

Quinine:			
Specialised drug store:			
Baseline	1.0 (3.0)	0.9 (2.7)	
Follow-up	3.4 (5.4)	4.2 (8.8)	-0.8 (-8.1, 6.5)
Mission_Private:			
Baseline	28.1 (36.8)	23.1 (34.3)	
Follow-up	11.5 (18.8)	22.2 (44.1)	-10.7 (-44.6, 23.1)
Government facility:			
Baseline	14.9 (19.4)	14.4(15.5)	
Follow-up	7.9 (10.1)	10.1 (5.2)	-2.2 (-10.2, 5.8)
General stores:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Other sources:			
Baseline	0 (0)	0 (0)	
Follow-up	3.2 (9.5)	1.9 (5.6)	1.3 (-6.5, 9.1)
Chloroquine:			
Specialised drug store:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0.5 (1.6)	-0.5 (-1.7, 0.6)
Mission_Private:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Government facility:			
Baseline	0.4 (1.3)	0.8 (2.4)	
Follow-up	0 (0)	0 (0)	0 (0,0)
General stores:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Other sources:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Artemisinin monotherapy:			
Specialised drug store:			
Baseline	0.4 (1.3)	0.4 (1.2)	
Follow-up	0 (0)	2.8 (8.3)	-2.8 (-8.7, 3.1)
Mission_Private:			
Baseline	0 (0)	3.7 (11.1)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Government facility:			
Baseline	1.2 (3.7)	5.6 (16.7)	
Follow-up	0 (0)	0.4 (1.3)	-0.4 (-1.4, 0.5)
General stores:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)
Other sources:			
Baseline	0 (0)	0 (0)	
Follow-up	0 (0)	0 (0)	0 (0,0)

Others includes receiving treatment at home with western medications and other health facilities not classified in the above such as army sanatoriums.

REFERENCES

Division of Malaria Control (DOMC) (2007) Transitional plan for implantation of Artemisinin-based combination therapy (ACT) malaria treatment policy in Kenya. Royal Pharmaceutical Management Plus.

APPENDIX 8

A8.1: Percentage of children aged 3-59 months receiving any brand of AL on the same day or following day of fever onset, by cluster

Cluster	Arm	Total number of U5 children-Baseline	Total no of U5 fevers-Baseline	Total no of fevers treated with AL[1] same or next day-Baseline	% of U5 treated with AL[1] on same or next day-Baseline	Total number of U5 children-Follow-up	Total no of U5 fevers-Follow-up	Total no of fevers treated with AL[1] same or next day-Follow-up	% of U5 treated with AL[1] on same or next day-Follow-up	Difference of mean between baseline and Follow-up
Akachachat	Control	116	46	2	4.3	104	27	8	29.6	25.3
Apokor	Control	146	55	1	1.8	144	50	9	18.0	16.2
Buchifi	Control	200	30	1	3.3	171	37	4	10.8	7.5
Kamunuoit	Control	135	30	2	6.7	149	28	7	25.0	18.3
Kanjala	Control	159	44	4	9.1	151	58	11	19.0	9.9
M.Central	Control	143	35	3	8.6	131	43	9	20.9	12.4
Musamba	Control	214	53	0	0.0	189	34	2	5.9	5.9
Nanderema	Control	156	43	4	9.3	156	42	16	38.1	28.8
Shianda	Control	112	17	1	5.9	110	25	3	12.0	6.1
Aludeka	Intervention	122	48	2	4.2	128	36	21	58.3	54.2
Eshibinga	Intervention	124	29	1	3.4	126	36	12	33.3	29.9
Kekalet	Intervention	143	45	2	4.4	149	51	25	49.0	44.6
Lunza	Intervention	151	25	2	8.0	157	35	10	28.6	20.6
Lupida	Intervention	166	68	7	10.3	166	79	34	43.0	32.7
Malaha	Intervention	187	36	0	0.0	195	30	9	30.0	30.0
Muyafwa	Intervention	183	61	5	8.2	170	58	30	51.7	43.5
Okatekok	Intervention	135	43	1	2.3	138	40	21	52.5	50.2
Sikinga	Intervention	157	58	1	1.7	128	52	30	57.7	56.0
Total		**2749**	**766**	**39**		**2662**	**761**	**261**		
Control total		1381	353	18		1305	344[2]	69		
Intervention total		1368	413	21		1357	417[2]	192		

[1]Refers to any brand of AL, including Tibamal®; [2]At follow-up, in the control arm 5 children had fever but information was missing on how the fever was treated, in the intervention arm 8 children had missing details on whether fever was present within 2 weeks prior to the interview.

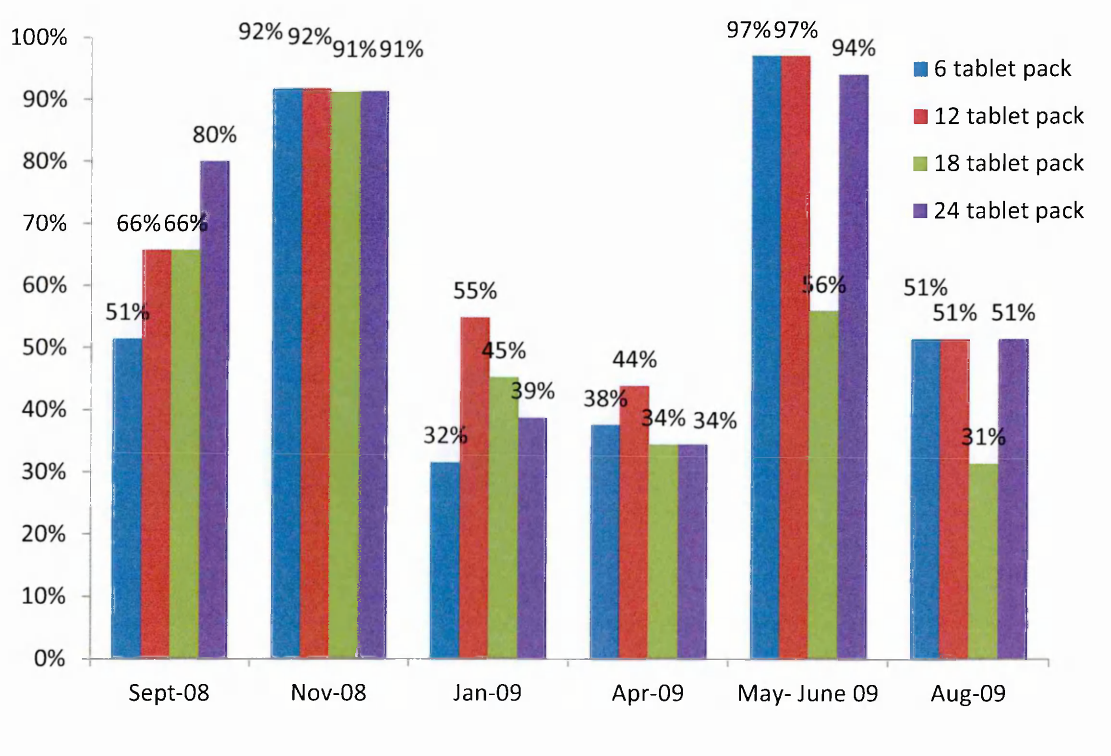
APPENDIX 9

AL SUPPLIES IN GOVENRMENT HEALTH FACILITIES

Supplies of AL at government health facilities were monitored during the study period, from September 2008 to August 2009. Calls were made to the pharmacy department of each facility every one to two months and information was collected on the availability of AL packs for the four patient weight groups of AL on the interview day, including details of any stock outs. The duration of any stock outs was detailed from respondents reviewing stock cards in the pharmacy.

Generally, supplies of AL in government health facilities during the study period tended to fluctuate. In September 2008, one month after baseline data collection was complete, supplies of the 6 tablet pack of AL were only available in half of health facilities. Details of AL supplies for April to August 2008, during baseline data collection activities, were not collected. However, interviews with members of the DHMTs and minutes of meetings during that time revealed complaints of severely low to non-existent supplies of AL. Towards the end of the year, there were generally sufficient supplies of all packs of AL, available in more than 90% of all facilities. AL availability in January and April 2009 was generally low, with the medication being available in less than half of facilities, but by the time of the start of follow-up data collection AL supplies had picked up again, with the 6, 12 and 24 packs found in more than 90% of facilities in May-June 2009, though by the end of data collection in August 2009, they had again fallen to around the 50% mark (Figure A9.1). The longest duration facilities were out of stock of AL was observed in April 2009 where facilities without AL remained out of stock for 32 to 89 days. More details on AL availability trends in Kenyan government health facilities and reasons for stock outs can be found in Kangwana *et al.,* (2009) and the MCH report (DOMC, 2010).

Figure A9.1: Availability of AL on Survey Day



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Kangwana BB, Njogu J, Wasunna B, Kedenge SV, Memusi DN *et al.*,(2009) Malaria drug shortages in Kenya: a major failure to provide access to effective treatment. Am J Trop Med Hyg. May;80(5):737-8.

Division of Malaria Control (DOMC), Kenya (2010) Monitoring Outpatient Malaria Case Management under the 2010 Diagnostic and Treatment Policy in Kenya.

APPENDIX 10

DOCUMENTATION OF CONTEXT

Data collection

Documentation of the context in which the survey took place was carried out in the form of a process evaluation, to identify possible external factors that may have influenced the study outcomes. Information was gathered from a variety of sources that included annual district health and budgetary reports from the study districts, minutes from stakeholder meetings held by the District Health Management Teams (DHMTs), proposals from organisations planning to carry out projects in the study districts, rainfall data from the district agricultural departments and formal and informal interviews with members from the DHMTs, DOMC in Nairobi, the PPB, and other relevant bodies. Data were collected at both baseline and follow-up and organised into a spreadsheet, using the following headings:

- Malaria related programs implemented in health facilities or in outlets supplying medication within the community
- Malaria related community awareness activities
- Changes in the number of health facilities
- Activities that may have affected the number of retailers selling medications
- Activities that may have affected the supply of antimalarial medications in government facilities
- Any companies promoting specific antimalarials within the community
- Unusual changes in patterns of malaria incidence in government health facilities
- Unusual changes in patterns of rainfall
- Anything else that might have affected treatment seeking behaviour for children suffering from malaria or fever

The spreadsheet was then reviewed to identify which factors may have had an effect on the study outcomes. These factors have been described below in two tables. Table A10.1 describes external influences likely to have had an effect on the intervention's outocmes and table A10.2 those that are likely not to have had an effect.

Table A10.1: External Influences Likely to Have Had an Effect on The Intervention's Outcomes

Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
Ministry of Health	1 facility was shut down	Busia, Butula division	2008/9- exact date unknown	The facility was located near a control study sub-location. This may have decreased the percentage of children with fever receiving appropriate treatment in the control arm, possibly increasing the difference observed between arms in percentage of children receiving appropriate treatment.
	Supplies of AL in government health facilities during the study period tended to fluctuate. More details of the availability of AL in these facilities can be found in appendix 9	All districts	Throughout the study period	Government supplies seemed to have been extremely low at baseline and have picked up at follow-up, across both arms. Increases in government supplies of AL post intervention may have improved appropriate treatment of childhood fevers in the control arm and decreased the demand for Tibamal® in the intervention arm as caregivers may have been more likely to use government facilities if they knew AL was available, and government facility staff may have been less likely to need to refer patients to Tibamal® outlets. Increased availability of AL occurred across both arms therefore any positive effects it may have had in the intervention arm would be cancelled out when compared to the control arm.
	The PPB regularly send teams out in to the community to identify and shut down retail outlets illegally selling medications. These crackdowns occurred across the study districts in an irregular pattern, prior to the study period and are still on-going. It was reported in Butere-Mumias that some of the targeted outlets selling Tibamal® and other medications were given notice to terminate stocking all other treatments other than Tibamal® which they had permission to sell.	All districts	Prior to the study period and still on-going	This activity may have possibly decreased the supply of other antimalarials, increasing the market share and possibly availability and use of Tibamal®. This activity may have enhanced the positive outcomes of the intervention.

Table continued on next page

Table A10.1 continued

Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
Ministry of Health	Pharmacy and Poisons Board-circulated letters to all importers, manufacturers, wholesale dealers, distributors and retailers, restricting the manufacturing, supply and selling of artemisinin monotherapies, SP and amodiaquine by the end of 2008.	All districts	Late 2007 early 2008	This activity may have possibly decreased the supply of other antimalarials, increasing the market share and possibly availability and use of Tibamal®. This activity may have artificially exaggerated the positive outcomes of the intervention.
Mentor Initative (an NGO)	Supplied extra supplies of AL to government health facilities to deal with potential increases in malaria prevalence caused by floods	Budalangi division in Busia	2008	This activity took place in a division where a control study sublocation was located. This activity may have increased the percentage of children with fever in the control arm receiving appropriate treatment. This activity may have decreased the difference in appropriate treatment observed between the arms, decreasing the observed impact of the intervention.

Table A10.2: External Influences Likely to Have Had No Effect on The Intervention's Outcomes

Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
Ministry of Health	Training of health care workers on national malaria treatment guidelines	All health facilities across all the study districts	Mid 2009	This may have improved the percentage of children with fever receiving appropriate treatment from baseline to follow-up. However the effect would have been observed across both treatment arms, and would have therefore not impacted on the intervention's outcomes.
	Training of CHWs to visit households and collect data on aspects such as births, immunization, HIV and malaria prevalence, and provide health information on diseases such as malaria. CHWs were initially given medications to treat minor ailments but more recently their role has been limited to referring those who need medical attention to health facilities	Across the districts of Butere and Mumias	On-going throughout study period	This activity may have increased the percentage of children with fever being treated in a government health facility, and possibly increased the percentage of childhood fevers being treated appropriately. However, the activity occurred in both intervention and control arms, therefore its effect on the intervention would have been controlled for in the study design and analysis.

Table continued on next page

Table A10.2 continued

Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
Ministry of Health	CHWs and pharmacy technicians educating households on good health seeking behaviour practices and adherence to medication	Teso district	Started prior to 2008 and is still on-going	This activity may have increased community members' knowledge and awareness of malaria, its treatment and adherence practices. However, the activity occurred across the whole of Teso district and occurred through both timepoints, and therefore its effect on the intervention would have been controlled for in the study design and analysis.
	Public health forums where communities come together to discuss general health issues.	Matayos division in Busia	Started prior to 2008 and is still on-going	This activity may have increased community members' knowledge and awareness of malaria and its treatment. This activity occurred in a division where an intervention sub-location was located. Since the forums took place both at baseline and follow-up, its effect on the intervention should have been controlled for in the study design and analysis.
	Functions held to celebrate World Malaria Day. The day usually involves public speeches made on communicating messages on aspects of malaria, and a net retreatment programme.	All districts	25^{th} April of each year	This activity may have increased community members' knowledge and awareness of malaria and its treatment. Since this day is celebrated across the whole country it is unlikely to have effect on the intervention outcomes; its effect on the intervention would have been controlled for in the study design and analysis.
	The public health department has had on going community barazas spreading health messages on various topics including malaria.	Across Mumias district	On going	This may have increased community members' knowledge and awareness of malaria and its treatment. This activity occurred across Mumias which had both intervention and control sublocations, therefore its effect on the intervention would have been controlled for in the study design and analysis.

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Table A10.2 continued

Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
AMREF (African Medical & Research Foundation)	Child survival project aimed at improving the quality of care received in the community focused on malaria, HIV and maternal and newborn care through: -capacity building through the training of community health care workers, traditional birth attendants and community midwives -The distribution of promotional items produced to support the project include t-shirts, bags and badges - CHWs are also provided with bicycles for outreach activities such as communicating health messages	The divisions of Butula and Funyala, Samia in Busia diatrict	Initiated prior to PhD study, on-going	This activity took place in areas where control sub-locations were located. One would expect to observe treatment of childhood fevers and caregivers knowledge of malaria to be better due to this activity. However since this activity was occurring both at baseline and follow-up, one would have expected its effects on the intervention to be controlled for in the study design and analysis.
	Education of school children and teachers on aspects of malaria	Teso and Busia district	Initiated prior to PhD study, still on-going	This activity would possibly increase knowledge of malaria and its treatment, possibly changing behavioural practices. However since the activity took place in both intervention and control areas throughout Teso and Busia one would have expected its effect on the intervention to be controlled for in the study design and analysis.
Ministry of Special Programmes in collaboration with the World Bank	Health education activities such as road shows, theatre groups, and radio shows. They also distributed IEC materials such as printed T-Shirts and subsidized ITNs to the community.	Butere-Shiatsala, and Eshibinga divisions in Butere Mumias district	June to July 2009	This activity took place during follow-up. One would expect it to have improved the community's knowledge on aspects of malaria that were included in the health education activities, however because this activity took place in divisions that had both intervention and control sub-locations it is unlikely that this activity would have affected the study outcomes. One would have expected its effect on the intervention to have been controlled in the study design and analysis.

Table continued on next page

Table A10.2 continued

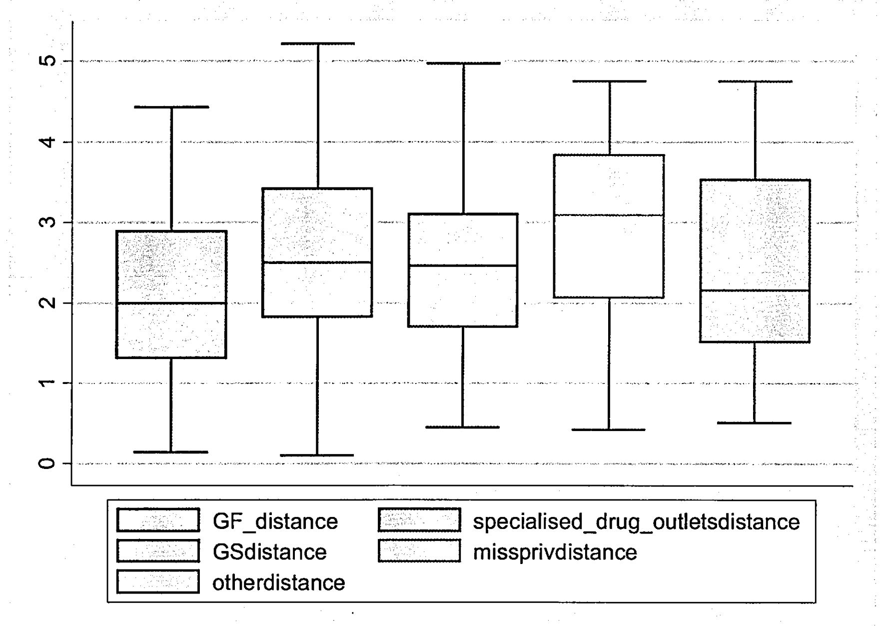
Organisation	Activity	Location	Timeline	Possible Effects on Interventions Outcome
Ministry of Special Programmes together with the Western Kenya Flood Mitigation Programme	Community sensitization programme on malaria prevention	Across Mumias district	April 2009	This activity may have resulted in a decreased prevalence of malaria cases at follow-up. However this would have been observed in both intervention and control arms and would most likely only have an effect on decreasing the sample size, however this effect was not observed in the analysis.
Family Health International	Running of a magnet theatre targeting the youth and mothers especially from low income countries, communicating messages of health mainly on HIV/ AIDS but also occasionally malaria	Teso district- Amogoro, Charcol and Amukura division	On-going throughout study period	One would have expected this activity to increase the community's knowledge and awareness of malaria. However, since it took place in divisions that contained intervention and control sub-location one would have expected its effect on the intervention to have been controlled in the study design and analysis.
SHEF (Sustainable Healthcare Foundation)	All Child and Family Wellness clinics (CFWs) which fall into the specialized drug stores category of the study, had already been trained on dispensing of ACTs as well as on other medications.	Across all districts	Prior to 2008	This activity would have improved knowledge of fever treatment in CFWs in the control arm above the 'usual' level of knowledge expected without training. However, this training occurred prior to the intervention roll out, and in both arms, so one would have expected its effect on the intervention to have been controlled in the study design and analysis.

APPENDIX 11

Analyses was carried out to assess whether caregivers' health seeking behaviour and providers' referral behaviours varied with their physical distance to the nearest public health facility. For caregivers' treatment seeking behaviour, the median distance of households to the nearest public health facility was assessed for each source of care that was sourced for children suffering from fever (refer to table 7.2). For providers' referral behaviour, the median distance of outlets to the nearest public health facility was assessed for each type of referral suggested for complicated malaria cases in children under five (refer to table 5.19).

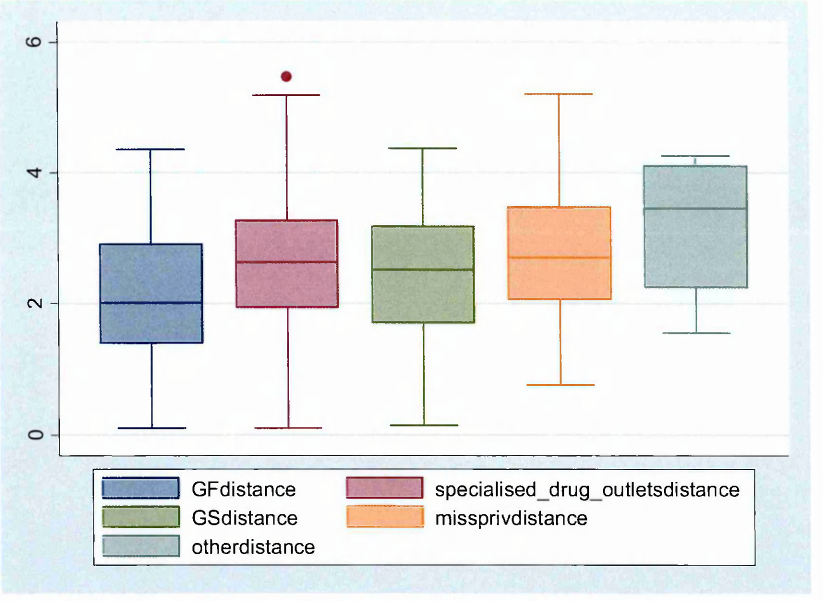
CAREGIVERS' HEALTH SEEKING BEHAVIOUR

Figure A11.1: Median distance (km) of household to nearest public health facility for caregivers seeking care at each outlet type. Baseline.



Median distances from the caregivers' household to the nearest public health facility, for caregivers who sourced care from different outlets: government health facilities (GF_distance)=2.0km; specialised drug outlet (spcialised_drug_outletdistance)=2.6km; general store (GSdistance)=2.5km; mission/ private health facility (missprivdistance)=3.1km; other=2.2km.

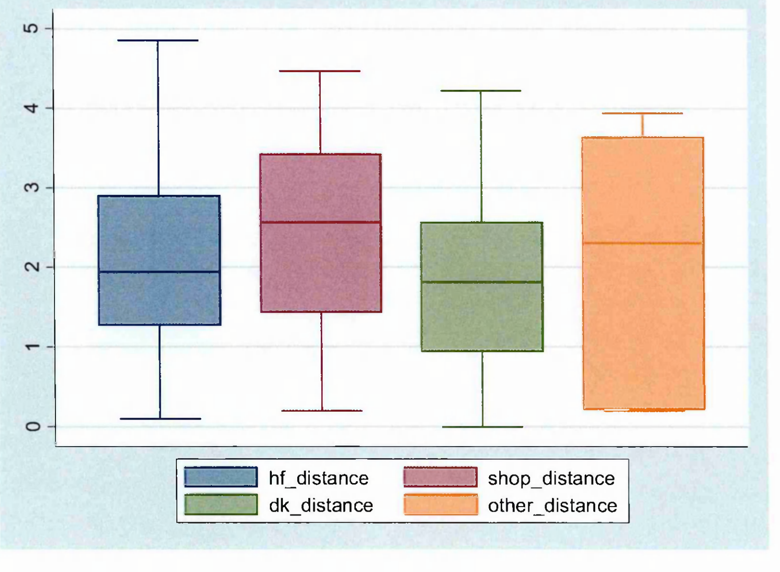
Figure A11.2: Median distance (km) of household to nearest public health facility for caregivers seeking care at each outlet type. Follow-up.



Median distances from the caregivers household to the nearest public health facility, for caregivers who sourced care from different outlets: government health facilities (GF_distance)=2.0km; specialised drug outlet (spcialised_drug_outletdistance)=2.6km; general store (GSdistance)=2.5km; mission/ private health facility (missprivdistance)=2.7km; other=3.4km.

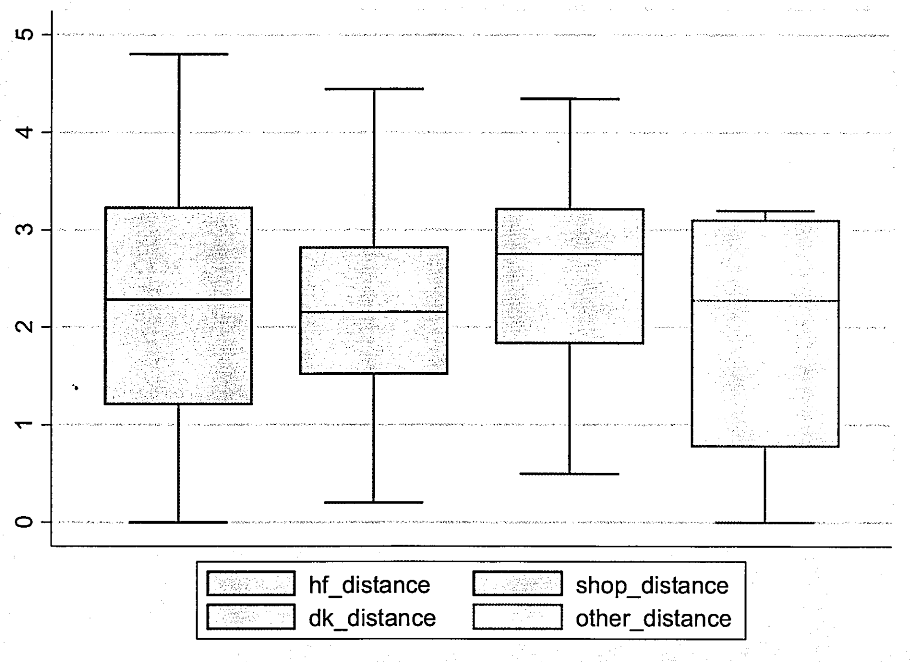
PROVIDERS' REFERRAL BEHAVIOURS

Figure A11.3: Median distance (km) of provider to nearest public health facility for providers stating that they would refer complicated cases to each outlet type. Baseline.



Median distances from the providers outlet to the nearest public health facility, for providers who would refer complicated cases to different sources of care: government health facilities (GF_distance)=1.9km; shop(shop_distance)=2.4km; would not know where to refer patient (dk_distance)=1.8km; other=2.3km.

Figure A11.4: Median distance (km) of provider to nearest public health facility for providers stating that they would refer complicated cases to each outlet type. Follow-up.



Median distances from the providers outlet to the nearest public health facility, for providers who would refer complicated cases to different sources of care: government health facilities (GF_distance)=2.3km; shop(shop_distance)=2.2km; would not know where to refer patient (dk_distance)=2.8km; other=2.3km.

APPENDIX 12

A separate 'difference in difference' analysis was carried out below on certain indicators from the mystery shopper survey (Chapter 6) and household survey (Chapter 7). A difference in difference analysis was carried out on indicators where baseline and follow data raised the possibility of a differential effect between the arms, but which did not necessarily appear to be of statistical significance. The analysis was carried out out by first calculating the difference between basleine and follow up for each cluster. Then a mean difference for the control and intervention arm was calculated. Finally, the difference in difference was obtained by calculating the difference between the mean difference in the control arm and the mean difference in the intervention arm, and an unpaired t-test was run assess the significance of the differences observed. In the difference in difference approach, adjustments are not made for covariates, so this analysis was carried out unadjusted. The analysis has been limited to tables 6.3, 6.6, 6.9 and 7.4. One limitation of the difference in difference analysis is that it is exposed to a phenomenon known as 'regression to the mean'. This is caused by random variation in the measured endpoints, where clusters with low observed values at baseline are expected to show an increase in the outcome value at follow-up and vice versa. Therefore it is generally preferred to control for baseline values by including it as a covariate in the analysis, as described in Chapter 4 in the methodology section (Hayes & Moutlon, 2009). The results below should therefore be interpreted with caution.

Table A6.3: Percentage of outlets where retailers asked whether the child had at least one sign of severe disease, using difference in difference analysis (mean of cluster summaries from the 9 intervention and 9 control clusters)

	Mean difference in control (N=9) % (SD)	Mean difference in intervention (N=9) % (SD)	Mean difference in difference (95% CI)	P-value Unadjusted
All outlets	0.9 (15.5)	10.6 (17.4)	9.7 (6.7, 26.2)	0.2283

Information based on outlets interviewed both for mystery shopper and provider survey.

Table A 6.6: Reasons given for not dispensing, of those retailers not dispensing any drugs, using difference in difference analysis (mean of cluster summaries from the 9 intervention and 9 control clusters) (multiple responses allowed)

Reasons for not dispensing any drug:	Mean difference in control (N=9) % (SD)	Mean difference in intervention (N=9) % (SD)	Mean difference in difference (95% CI)	P-value Unadjusted
No drugs in stock	10.8 (20.6)	-16.5 (26.0)	-27.3 (-50.8, -3.8)	0.0253
No antimalarials in stock	10.0 (8.4)	23.8 (15.6)	13.7 (1.1, 26.3)	0.0343
No suitable drugs in stock[1]	14.0 (19.0)	13.7 (24.4)	-0.3 (-22.1, 21.5)	0.9768
Referred to a specialized drug store	2.9 (27.1)	4.4 (24.0)	1.6 (-24.0, 27.1)	0.8991
Referred to a health facility	4.8 (27.1)	-7.6 (21.5)	-12.4 (-36.9, 12.0)	0.2979

[1]Shopkeeper said they had no suitable drugs in stock which generally meant that either they did not feel they had appropriate drugs to treat the stated symptoms, or that they did not have appropriate drugs to treat children of the stated age (4 years)

Table A6.9: Specific antimalarials dispensed by retailers, using difference in difference analysis (mean of cluster summaries from the 9 intervention and 9 control clusters)

Anitmalarials dispensed:	Mean difference in control (N=9) % (SD)	Mean difference in intervention (N=9) % (SD)	Mean difference in difference (95% CI)	P-value Unadjusted
AL	1.2 (1.9)	25.4 (6.9)	24.1 (19.1, 29.2)	0.0001
Tibamal®	0 (0)	24.4 (7.0)	24.4 (19.5, 29.3)	0.0001
Amodiaquine	-11.7 (7.9)	-23.5 (12.4)	-11.9 (-22.2, -1.5)	0.0274
SP	3.1 (9.6)	-5.0 (10.3)	-8.1 (-18.1, 1.8)	0.1036
Quinine	1.9 (2.5)	1.9 (3.3)	0.0 (-2.9, 2.9)	0.9999
Other drugs[1]	0.4 (3.2)	0.3 (3.9)	-0.1 (-3.7, 3.4)	0.9299

[1] Other drugs are non-antimalarials and non-antipyretics and include: Antibiotics (Amoxicillin, Cotrimoxazole and Trimethoprim), Antihistamines (Chlorpheniramine), Antihelminthics (Levamisole), and Bronchodilators (Salbutamol).

Rank sum test: unadjusted analysis, p=0.0003; adjusted analysis, p=0.0003. This test was carried out on the main outcome indicator because of its robustness and its sensitivity to any shifts in distribution between control and intervention clusters. (Hayes & Moulton, 2009)

Table A7.4: Anti-malarial treatment obtained for children aged 3-59 months with fever in the previous two weeks, using difference in difference analysis (a comparison of the 9 intervention and 9 control clusters)

Treatment seeking behaviour indicators	Mean difference in control (N=9) % (SD)	Mean difference in intervention (N=9) % (SD)	Mean difference in difference (95% CI)	P-value Unadjusted
Children who received an antimalarial	11.4 (8.6)	18.5 (12.4)	7.1 (17.8, -3.5)	0.1740
Children who received an antimalarial monotherapy	-7.0 (11.8)	-26.6 (9.5)	-19.6 (-8.9, -30.3)	0.0013
Children who received any brand of AL	17.1 (13.9)	45.8 (13.6)	28.7 (42.4, 15.0)	0.0004
Children who received any brand of AL on the same day or following day of fever onset	14.5 (8.4)	40.2 (12.4)	25.7 (36.2, 15.1)	0.0001

Total number of children with fever in the previous two weeks present in the control arm: Baseline=353; Follow-up=344
Total number of children with fever in the previous two weeks present in the intervention arm: Baseline=413; Follow-up=417
SD= standard deviation, CI=confidence interval, N= number of clusters

REFERENCE

Hayes RJ & Moulton LH (2009) Cluster Randomised Trials. Boca Raton: CRC Press.